Chemistry and Life

An Introduction to General, Organic, and Biological Chemistry

John W. Hill
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Surjeet Publications

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Preface

Why write a book?

Arnold Toynbee, British historian and author, says that the "only good reason . . . is because one's wish to write it is a master passion." We have experienced that desire. But writing is also hard work. A consuming passion must come from an important purpose. What is our purpose in writing this book? After all, there are other chemistry texts available for the life and health sciences. Briefly, we have set out to give you a book which:

Is readable, enjoyable. We feel that a chemistry text need not be stodgy in order to present good chemistry. Learning chemistry isn't easy, but it can be fun. A text can be readable and enjoyable. The use of humor at appropriate points can add to the excitement and satisfaction of learning.

Is consistently and directly related to life. Most texts do relate the biochemistry sections to the health and life sciences. We feel that all the basic principles and the inorganic chemistry as well, throughout the book, should also be related to life and living.

Has abundant examples, worked out in detail. We have provided sample problems, with detailed solutions, wherever appropriate throughout the text. These make both teaching and learning easier and more enjoyable.

Is a thoroughly integrated text. The text is extensively cross-referenced. In early chapters on chemical principles, we anticipate biological applications. These are then fully developed in subsequent chapters.

Explains difficult concepts in detail. Students don't have to depend on a collection of words alone to gain an understanding of abstract concepts. The drawings, diagrams, and photographs used render abstractions less formidable. Analogies drawn from everyday life illustrate concepts.

Is designed for future professionals yet has a strong liberal arts component. Health and life science professionals need a sound course in chemistry, but they will also be citizens. We have provided material on drugs, pollution, bioethics, and similar topics to help our future professionals be better-informed citizens.

Provides a liberal selection of problems at the end of each chapter. Students can immediately check their understanding of the material. Answers to selected problems are given in appendix D.

Presents references and suggestions for further reading. At the end of each chapter, books and articles are listed. Students whose interest has been kindled can delve more deeply into the subject.

Uses units most likely to be encountered in professional practice. Health professionals in the United States are in the last stages of the transition from the British and apothecary systems to the metric system. At the same time, the use of SI units is increasing in international scientific circles. We have retained many of the familiar "old" metric units such as *calorie* for energy and *millimetres of mercury* for pressure. These units are easy to visualize and will continue in use among many chemists and health and life scientists for years to come. On the other hand, we have used international spellings (*litre,* not *liter*) and symbols (K, not °K) where these do not present a barrier to learning.

Is exceedingly flexible. This book contains optional material that can be selected to suit individual needs. You can tailor a course to best serve your students. The book provides ample material for a full year's course. Suggested outlines for shorter courses of one semester (and for one or two quarters) are included in the *Instructor's Guide.*

Uses tested and tried methods for presenting materials. The approach that we have chosen has been proved sound in practice for a broad spectrum of students with widely varying backgrounds, both at private liberal arts colleges and at open-admissions state-supported schools. Students still have to study, but their study will be rewarded with success. We believe that any student, even one with modest preparation, can succeed if he or she invests time in the study of these materials.

Is designed to aid teachers. We, like you, never seem to have enough time to teach all the things that we would like to in a chemistry course. We have designed this book as an aid to the teacher. No book—or other educational device—can ever replace the classroom teacher. We are confident, though, that you will find this book easier to teach from than the usual text, because we have used only those techniques that have worked best for us in our classrooms.

We would like to thank all of those who helped with this work. Thanks to C. A. VanderWerf, who read the entire manuscript and made many helpful suggestions. We are indebted to Patti Organ, a student at Saint Mary's, who also read every word of the manuscript. A special thanks to Alanna Lucas, a typist who knows chemistry and who caught some of our errors. Cindy Hill provided the originals of several drawings and read some of the chapters. We especially want to thank our editor, Bob Lakemacher, for his patience, kindness, and good humor throughout.

Your comments, corrections, suggestions, and criticisms are eagerly solicited.

To the Student

What is chemistry?

Chemistry is such a broad, all-encompassing area of study that people almost despair in trying to define it. Indeed, some have taken a cop-out approach by defining chemistry as "what chemists do." But that won't do; it's much too narrow a view.

Chemistry is what we all do. We bathe, clean, and cook. We put chemicals on our faces, hands, and hair. Collectively, we use more than 10 000 consumer chemical products in our homes. Professionals in the health and life sciences use thousands of additional chemicals as drugs, antiseptics, or reagents for diagnostic tests.

Your body itself is a remarkable chemical factory. You eat and breathe, taking in raw materials for the factory. You convert these supplies into an unbelievable array of products, some incredibly complex. This chemical factory—your body—also generates its own energy. It detects its own malfunctions and can regenerate and repair some of its component parts. It senses changes in its environment and adapts to these changes. With the aid of a neighboring facility, this fabulous factory can create other factories much like itself.

Everything you do involves chemistry. You read this sentence; light energy is converted to chemical energy. You think; protein molecules are synthesized and stored in your brain. All of us are chemists.

Chemistry affects society as well as individuals. Chemistry is the language—and the principal tool—of the biological sciences, the health sciences, and the agricultural and earth sciences.

Chemistry has illuminated all of the natural world, from the tiny atomic nucleus to the immense cosmos. We believe that a knowledge of chemistry can help you. We have written this book in the firm belief that beginning chemistry can be related immediately to problems and opportunities in the life and health sciences. And we believe that this can make the study of chemistry interesting and exciting, especially to nonchemists.

For example, an "ion" is more than a chemical abstraction. A mercury ion in the wrong place can kill you, but a calcium ion in the right place can keep you from bleeding to death. "$P \times V = c$" is an equation, but it is also the basis for the respiratory therapy which has saved untold lives in hospitals. "Hydrogen bonding" is a chemical phenomenon, but it also accounts for the fact that a dog has puppies while a cat has kittens and a human has human offspring. Hundreds of similar fundamental and interesting applications of chemistry to life can be cited.

A knowledge of chemistry has already had a profound effect on the quality of life. Its impact on the future will be even more dramatic. At present we can control diabetes, cure some forms of cancer, and prevent some forms of mental retardation because of our understanding of the chemistry of the body. We can't *cure* diabetes or cure *all* forms of cancer or *all* mental retardation, because our knowledge is still limited. So learn as much as you can. Your work will be enhanced and your life enriched by your greater understanding.

Be prepared. Something good might happen to you—and to others because of you.

Contents

chapter 1 Matter and Measurement 1
2 Atoms 16
3 Nuclear Processes 47
4 Chemical Bonds 80
5 Energy and Equilibria 103
6 Gases 127
7 Liquids and Solids 146
8 Oxidation and Reduction 165
9 Solutions 183
10 Acids and Bases 206
11 More Acids and Bases 223
12 Electrolytes 238
13 Bioinorganic Chemistry 256
14 Hydrocarbons 279
15 Halogenated Hydrocarbons 313
16 Alcohols, Phenols, and Ethers 335

chapter **17** Aldehydes and Ketones 358
18 Organic Acids and Derivatives 375
19 Amines and Derivatives 400
20 Compounds of Sulfur and Phosphorus 425
21 Polymers 440
22 Carbohydrates 458
23 Lipids 473
24 Amino Acids and Proteins 493
25 Nucleic Acids 515
26 Enzymes and Coenzymes 532
27 Vitamins and Hormones 547
28 Body Fluids 569
29 Digestion 586
30 Carbohydrate Metabolism 597
31 Lipid Metabolism 617
32 Protein Metabolism 637
appendix **A** The International System of Measurement 653
B Exponential Notation 655
C Solving Problems by Dimensional Analysis 657
D Answers to Selected Problems 659
index 663

chapter 1

Matter and Measurement

This book is called *Chemistry and Life.* What does chemistry have to do with life? What is chemistry? For that matter, what is life?

The last question is more than rhetorical. Progress in science, technology, and medicine has blurred the distinction between life and death. Is someone whose heart has stopped beating dead? Is someone whose vital functions are being maintained by machine alive? We won't even attempt in this book to supply a definitive answer to the question "What is life?" We'll simply note its critical significance for our society.

How about the first question, "What does chemistry have to do with life?" A chemist would say, "Just about everything." The human body, for example, is the most extraordinarily complicated, most elegantly designed, and most efficiently operated chemical laboratory there is. Our attempt to answer that first question will fill most of this text.

That leaves the middle question, "What is chemistry?" And that is the subject of this first chapter. We shall see how science in general and chemistry in particular have developed from earlier human endeavors. Our study will include a consideration of the methods of science and the manner of its progress. Finally, we shall also develop some basic concepts necessary to our study of chemistry and its relationship to life.

1.1 Science and the Human Condition

We are taught in elementary school that people have three basic needs: food, clothing, and shelter. Certainly those three things—if adequate in quantity and quality—are enough to keep us alive. Most of us, however, would also agree to adding two more requirements for the good life: reasonable health and some chance for happiness.

In early human societies, nearly all human efforts were directed toward the hunting and gathering of food, the making of clothing, and the provision of shelter. Our early ancestors had no knowledge of the biological

Figure 1.1 *The Alchemist,* a painting done by the Dutch artist Cornelis Bega around 1660, depicts a laboratory of the 17th century. (Courtesy of Aldrich Chemical Company, Milwaukee.)

Figure 1.2 Theophrastus Bombastus von Hohenheim, better known as Paracelsus. (Courtesy of the National Library of Medicine, Bethesda, Md.)

and chemical bases of illness, and there was little they could do about their health except to pray and make sacrifices to their gods. With the coming of civilization, some people gained enough leisure to turn their thoughts to the human condition and to the natural world around them. Over the centuries what we now call science grew out of their speculations. As this scientific study of the material universe progressed, the responsibility for adding to the growing body of knowledge was divided among various disciplines. Among these disciplines was chemistry.

Modern chemistry's roots are firmly planted in alchemy, a kind of mystical chemistry which flourished in Europe during the Middle Ages. And modern chemists have inherited from the alchemists an abiding interest in those aspects of their study that relate to human health and to the quality of life.

Consider, for example, the fact that alchemists not only searched for a "philosopher's stone" that would turn cheaper metals into gold but also sought an "elixir" that would confer immortality on those exposed to it. Alchemists never achieved their primary goals, but they did discover many new chemical substances. As early as the ninth century, a Persian alchemist, Al-Razi, described the use of plaster of Paris for casts to set broken bones. And alchemists perfected techniques such as distillation and extraction that are still useful in our time.

It was a Swiss physician, Theophrastus Bombastus von Hohenheim (1493–1541), who urged alchemists to turn away from their attempts to make gold and to seek instead medicines with which to treat disease. Possessed of a monstrous ego, von Hohenheim (who preferred the self-chosen name Paracelsus) alienated many of his contemporaries. His followers, however, were numerous enough to ally forever the science of chemistry with the art of medicine.

By the 17th century, a changed attitude, characterized by a reliance on experimentation, had been adopted by astronomers, physicists, physiologists, and philosophers. It was this change in orientation that signaled the emergence of chemistry from alchemy. The English philosopher Sir Francis Bacon (1561–1626) had visions of these new scientific methods endowing human life with new inventions and wealth.

By the middle of the 20th century, it appeared that science and its application in technology had made the dreams of Bacon and von Hohenheim a reality. Many diseases had been virtually eliminated. The coordination of chemistry and medicine had also made the difference between operations in which four strong men were employed to hold the patient down and ones in which the patient was painlessly anesthetized. Fertilizers, pesticides, and scientific breeding had made food more abundant. Nutritionists were applying their science to designing diets that would produce healthier, stronger people. New materials were being developed to improve our clothing and shelter. Industry was offering an almost endless variety of products at relatively low cost to the average consumer.

Indeed, it seemed that, despite its sometimes less than honorable intentions, science could do no wrong. For example, during World War I, when the German armies' supply of ammonia (which they needed to make nitrate explosives) was cut off, the Haber process provided them with an alternate supply. Fritz Haber's work probably lengthened the war, but it is far more significant for its influence on modern agriculture. Ammonia and nitrates are the stuff of which fertilizers are made, and fertilizers are essential to modern high-yield farming. In fact, most of the ammonia made by the Haber process today goes into fertilizer.

Much of the technology of the mighty 20th century had grown out of scientific discoveries. New technological developments were used in turn by scientists as tools to make new discoveries. These developments in science and technology became hallmarks of the modern world. Hardly anyone questioned that science in the early part of the 20th century had significantly improved the human condition.

Figure 1.3 Sir Francis
English philosopher and
Chancellor to James I.
(Duplication courtesy of
Smithsonian Institution,
Washington, D.C.)

1.2 Problems in Paradise

If during the first half of the 20th century science was viewed as humankind's savior, during the latter half it is being viewed as quite the opposite. Those anesthetics that made surgery painless for the patient have caused female anesthesiologists, surgeons, and surgical nurses to suffer a high percentage of miscarriages compared to other health personnel. Fertilizer runoff from farms has polluted streams, and insecticide residues have had a devastating effect on wildlife. Some of those industrial workers making modern products for our use have died from diseases caused by the chemicals they worked with.

One solution to these problems would be simply to throw out science. But do we really wish to return to surgery without anesthetics? Most of us don't. We need scientists, for it is they who will search for safer anesthetics, for approaches to increased agricultural production compatible with the natural environment, and for analytical techniques which will ensure healthful working conditions for industrial personnel.

The simple fact is that chemistry and its products, both good and bad, are so intimately involved in determining the quality of life that to ignore the subject is to court disaster. It will take an educated, informed society to ensure that science is used for the human good.

Figure 1.4 Fritz Haber,
German chemist who inv
a process for manufactur
ammonia. (Courtesy of
Encyclopaedia Britannica
Chicago.)

1.3 The Way Science Works—Sometimes

Textbooks often define science as a "body of knowledge," and it is frequently taught as a finished work rather than an ever-changing approach to learning. Science is organized into concepts. For example, even though we will often speak of atoms as if they were readily observed, the atomic concept is merely a convenience which successfully describes many observable facts in a metaphorical way. It is not the "body of facts" that characterizes science but the *organization* given to those facts. To be useful, concepts must have predictive value. If the atomic theory is to be useful, it should enable a scientist to predict how matter will behave.

The most distinguishing characteristic of science is its use of processes or methods. The making of observations and the cataloguing of facts are bare, though necessary, beginnings to these intellectual processes. Scientists must be able to make careful measurements, but they must also be able to

Scientists use the word *model* somewhat differently than nonscientists. A scientific model helps one "visualize" the invisible. For example, when a glass of water is allowed to stand for a period of time, the water apparently disappears. This process is called *evaporation*. Scientists explain this phenomenon by means of a model referred to as the *kinetic-molecular theory*. According to this theory, the liquid is made up of small, invisible particles called molecules. These molecules are in constant motion. In the bulk of the liquid, each molecule is surrounded on all sides by other molecules. These molecules can bump back and forth against one another, but because they are totally surrounded they are trapped. However, for a molecule at the surface, there is the possibility of escape. If one molecule is hit hard enough by another molecule, the first can be knocked free of the surface. It then becomes part of the air, which is simply another collection of molecules. The air, unlike the liquid, is a gas in which all the molecules are very far apart. They are so far apart that essentially all light passes right through them, so they can't be seen; thus, the water disappears. It is far more satisfying for the scientist to understand evaporation by means of a model such as this than merely to have a name for the process.

grasp the central theme of these observations. They must recognize the variables and be able to note the effect of changing one variable at a time. Scientists must be able to sort out the useful aspects of information and ignore irrelevancies. Perhaps basic to these intellectual processes is the ability to formulate testable hypotheses. Even an educated guess is of little value to scientists unless an experiment can be devised to test the guess. Successful scientists can deduce evidence from a model. Truly outstanding scientists may invent original models.

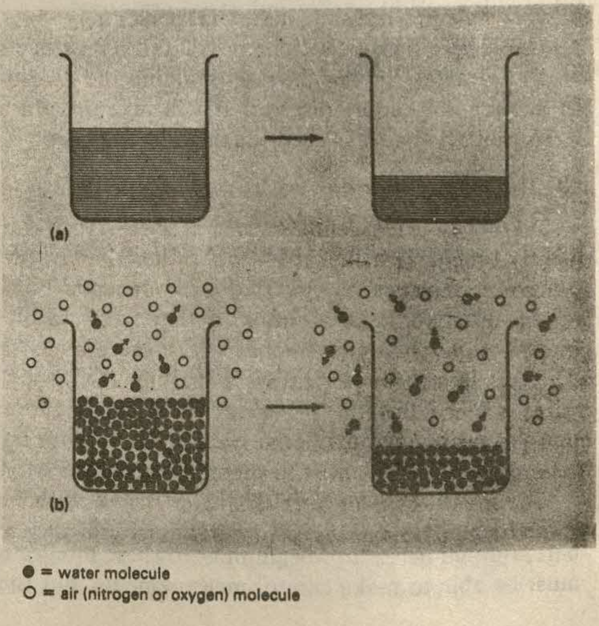

Figure 1.5 The evaporation of water. (a) When a container of water is left standing open to the air, the water slowly disappears. (b) Scientists explain evaporation in terms of the motion of molecules.

Science is not totally different from other disciplines. For example, creativity is central to both science and the humanities. Science does not involve cold logic to the exclusion of other human characteristics. Albert Einstein recognized that there was no *logical* path to some of the laws that he formulated. Even he relied on intuition based on experience and understanding.

It is important that you realize there is no single "scientific method" which, when followed, produces guaranteed results. Scientists observe, gather facts, and make hypotheses, but somewhere along the way they test their hunches and their organization of facts by experimenting. Scientists, like other human beings, use intuition and may generalize from a limited number of facts. Sometimes they are wrong. One of the strengths of science lies in the fact that results of experiments are published in scientific journals. These results are read—and often checked—by other scientists in all parts of the world. To become an accepted part of the "body of knowledge," the results must be reproducible. Scientists also extend each other's work, sometimes to the point that we see a "bandwagon" effect. One breakthrough sometimes results in the unleashing of vast quantities of new data and leads to the development of new concepts. For example, early in the 19th century it was thought that certain chemical substances, called *organic* compounds, could be produced only by living tissue, such as someone's liver or the leaf of a plant. These substances were in contrast to other materials, labeled *inorganic*, which could be prepared by a chemist in a laboratory. In 1828, a German chemist named Friedrich Wöhler (1800–1882) succeeded in making an organic compound from an inorganic one in the laboratory. The belief that such a compound could not be prepared in this manner was so strong that Wöhler did the same thing over and over again to assure himself that he had really done the "impossible." When he finally published his work, other chemists quickly repeated it and then proceeded to make hundreds of thousands of organic compounds. That bandwagon is still rolling today, with chemists making hormones, vitamins, and even genes in the laboratory.

Thus, contrary to an often-expressed popular notion, scientific knowledge is not absolute. Science is cumulative, and the "body of knowledge" is dynamic and constantly changing. Old concepts or even old "facts" are discarded as new tools, new questions, and new techniques reveal new data or generate new concepts. To truly understand what science is, one has to observe what the whole, worldwide community of scientists has done over a period of several years rather than look over the shoulder of a single scientist for a few days.

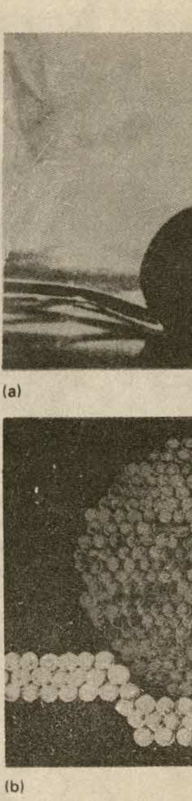

Figure 1.6 (a) A s
striking the surface c
liquid. (b) How a sc
might visualize the p
terms of an atomic n
(Courtesy of Dow C
Corporation, Midlan

1.4 What Is Chemistry? Some Fundamental Concepts

Nowadays, chemistry is often defined as a study of matter and the changes that it undergoes. Changes in matter are accompanied by changes in energy. Since the entire universe is made up of nothing more than matter and energy, the field of chemistry extends from atoms to stars, from rocks to living organisms. Matter and energy are such fundamental concepts that definitions are difficult. *Matter* is the stuff which makes up all material

Figure 1.7 An astronaut who weighs 80 kg on earth is "weightless" in space. His mass (quantity of matter) is constant, however. (Courtesy of the National Aeronautics and Space Administration, Washington, D.C.)

things. It occupies space and has mass. Wood, sand, water, and people have mass and occupy space. So does air, although one usually needs a flat tire or a 30-mi/hour wind to emphasize the point. *Mass* is a measure of the quantity of matter. *Weight,* on the other hand, is a measure of how strongly an object is attracted by the earth. On the earth's surface, weight is proportional to mass, and those two terms may be used interchangeably for most purposes. In space, however, an astronaut would have the same mass (i.e., the same quantity of matter) as on earth but would have no weight (because the pull of the earth's gravity is canceled while the spaceship circles the earth). Weight is determined by gravity; mass is invariant.

Matter comes in three familiar states: solid, liquid, and gas. Solid objects generally maintain their shape and volume regardless of their location. Many solids are crystalline in nature. Liquids assume the shape of their containers (except for a generally flat surface at the top). Like solids, however, liquids maintain a fairly constant volume. Unlike solids, they flow rather readily. Gases maintain neither shape nor volume. Rather, they expand to fill completely whatever container one puts them in and can be easily compressed. For example, enough air for many minutes of breathing can be compressed into a steel tank for underwater diving. We shall consider the states of matter in considerably more detail in later chapters.

Energy is often defined as the capacity for doing work. (By this definition, play involving exercise is called work.) But energy is more than that. It is the basis for change in the material world. When something moves or breaks or cools or shines or grows or decays, energy is involved. Energy is usually divided into two general categories, *potential* and *kinetic.* A system has potential energy by virtue of its position, that is, simply by being in a particular arrangement or place. The usual example given for such a system is a boulder on a cliff. Simply because it is at the top of the cliff and not at the bottom, the boulder has potential energy, which it can use to do work. The boulder can fall from the cliff and destroy a house at the base (thereby doing work), whereas a similar boulder sitting at the base of the cliff cannot do the same thing.

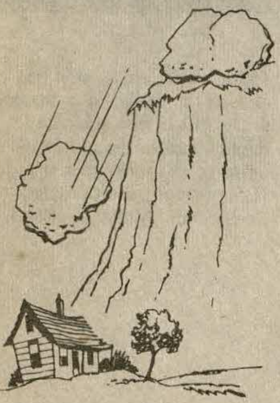

Figure 1.8 A boulder on a cliff represents potential energy. A falling boulder represents kinetic energy. The falling boulder can do work (smash a house, for example). The boulder on the cliff has a potential for doing the same thing.

Kinetic energy is energy in motion. The boulder that was sitting at the base of the cliff could destroy the house if it were rolling along the ground at a good clip. Its ability to do work in this case would depend on its motion. If you were really determined to destroy that poor house using kinetic energy, your best bet would be to use a large boulder rather than a small stone. Given the choice, it would also be better to get it moving at a brisk rather than a leisurely pace. That is just another way of saying that kinetic energy depends on mass and velocity. The bigger an object is and the faster it is moving, the more kinetic energy it has and the more work it can do.

In addition to the two major categories described above, energy is sometimes divided into a number of subcategories. These classifications are based on some characteristic of the energy being considered, for example, its source. It is easier to discuss some of these various types of energy by indicating their significance in the overall pattern of energy flow on earth.

The source of nearly all the energy on earth is the sun. Solar energy radiates through space as light. A small portion of this *radiant energy* reaches the earth, where some of it is converted to *heat energy*. This heat causes water to evaporate and then rise to form clouds. The water in the clouds has potential energy. As the water falls through the air and then flows in rivers, the potential energy is converted to kinetic energy.

The kinetic energy of the flowing stream can be used to turn a turbine, which converts a part of the stream's energy to *electrical energy*. The electricity thus produced can be transported by wires to homes and factories, where it is converted to light energy or to heat or to still other forms of energy.

Some of the solar energy striking the earth is absorbed by green plants, which use a complicated chemical process called *photosynthesis* to convert solar energy into *chemical energy*. The chemical energy stored by plants—now and in ages past—is used by humankind for food and fuel. Nearly all the vast quantities of energy used in our modern civilization come ultimately from the sun by way of green plants. Plants of the current age are harvested in forestry and agriculture. Those of ancient ages are reaped as fossil fuels—coal, oil, and gas.

One form of energy not attributable to the sun is nuclear energy. This type of energy was stored in the earth's crust when the solar system was formed some 4 or 5 billion years ago. We recover it for use or misuse when we mine uranium and build nuclear reactors or atomic bombs.

But chemistry is not concerned only with matter and its changes. It is also concerned with the energy transformations that accompany these changes. To deal with energy transformations, chemistry often borrows fundamental concepts from its neighboring discipline, physics. One such concept is *force*. A force is a push or a pull that sets an object in motion, or stops a moving object, or holds an object in place. *Gravity* is a force. Objects—including us—are held to the surface of the earth by gravity, the attraction of its mass for our mass. The weight of an object is the force of gravity that exists between it and the earth.

Electrical forces are extremely important in chemistry. Particles of matter bear two types of electrical charges, called positive (+) and negative (−). No one can really tell you exactly what an electrical charge is. We simply accept the fact that a particle with a "charge" can exert a force, that is, can

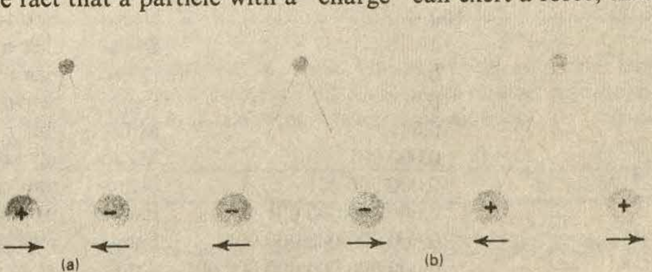

Figure 1.9 (a) Particles with unlike charges attract one another. (b) Those with like charges repel one another.

push or pull another particle which also has a "charge" on it. The particles do not have to be touching one another to attract or repel. For this reason, we say charged particles have force fields about them. Even at a distance they attract and repel one another, although these forces get weaker as the particles get farther apart. Particles with like charges (both positive or both negative) repel one another. Those with unlike charges (one positive and one negative) attract one another.

Figure 1.10 Static cling.

This phenomenon of charged substances is not unfamiliar to you. Anyone who has pulled clothes from an automatic dryer on a cold winter's day has probably seen what commercials like to call "static cling," pieces of clothing sticking to one another. The "cling" is due to the attraction of *unlike* charges. If, on the other hand, you brushed your hair vigorously on this same cold day, it might have become "unmanageable" (another great commercial term). Instead of lying flat against your head, it may have stuck out, each strand seemingly trying to get away from all the other strands. And that is exactly what was happening. The strands had *like* charges on them and were repelling one another.

1.5 Measurement: The Metrics Are Coming!

Accurate measurement of such quantities as mass (weight), volume, time, and temperature are essential to the compilation of dependable scientific "facts." Such facts may be used by a chemist interested in basic research, but similar information is of critical importance in every science-related field. Certainly we are all aware that measurements of both temperature and blood pressure are routinely made in medicine. It is also true that modern medical diagnosis depends on a whole battery of other measurements, including careful chemical analyses of blood and urine.

Table 1.1
Approved numerical prefixes

Exponential Expression	*Decimal Equivalent*	*Prefix*	*Phonic*	*Symbol*
10^{12}	1 000 000 000 000	Tera-	ter a	T
10^{9}	1 000 000 000	Giga-	ji′ ga	G
10^{6}	1 000 000	Mega-	meg a	M*
10^{3}	1 000	Kilo-	kil′ o	k*
10^{2}	100	Hecto-	hek′ to	h
10	10	Deka-	dek′ a	da
10^{-1}	0.1	Deci-	des′ i	d
10^{-2}	0.01	Centi-	sen′ ti	c*
10^{-3}	0.001	Milli-	mil′ i	m*
10^{-6}	0.000 001	Micro-	mi′ kro	μ*
10^{-9}	0.000 000 001	Nano-	nan′ o	n
10^{-12}	0.000 000 000 001	Pico-	pe′ ko	p
10^{-15}	0.000 000 000 000 001	Femto-	fem′ to	f
10^{-18}	0.000 000 000 000 000 001	Atto-	at′ to	a

*Designates most commonly used units.

A variety of systems of measurement are currently in use in the United States and around the world. The "British" system of feet, pounds, and quarts has been used in this country and in Canada and the United Kingdom. All three nations are now committed to changing to the *metric system.*

There are less familiar systems which serve specialized groups. Apothecary weights, for example, were used by pharmacists and in some hospitals, but these units are also being discarded in favor of the metric system. The single drawback to this otherwise laudable change is that we shall forever lose the "scruple" as a unit of measure.

Scientists around the world have long used the metric system. More recently, scientists have adopted an updated metric plan called the International System of Measurements, or SI (from the French Système International).

The beauty of the metric system and SI is that they are based on the decimal system, which makes converting from one unit to another rather simple—as we shall see. The basic unit of length is the metre; a convenient unit of mass (weight) is the gram; and a convenient unit of volume* is the litre. All other units are derived from these by the use of prefixes. For example,

1 millimetre (mm) = 0.001 metre (m)
1 milligram (mg) = 0.001 gram (g)
1 millilitre (ml) = 0.001 litre (ℓ)
1 kilogram (kg) = 1000 grams (g)
1 kilometre (km) = 1000 metres (m)

If you are not familiar with the SI, you might find the following British equivalents helpful for establishing in your mind the "size" of the SI units.

1 m = 39.4 in., or 1.09 yd
1 ℓ = 1.06 qt
1 kg = 2.2 lb

Conversions from one unit to another within the metric system are much easier than those within the British system.**

Example 1.1 Convert 0.74 kg to grams.

$$0.74\ \text{kg} \times \frac{1000\ \text{g}}{1\ \text{kg}} = 740\ \text{g}$$

---

*Volume may be expressed as length cubed. The SI unit of volume is the cubic metre (m^3). A more convenient unit for us is the cubic centimetre (cm^3). The symbol cm^3 is also read (and written) sometimes as "cc." Note that 1 ml = 1 cm^3.

**If you are unfamiliar with the use of conversion factors or would like to review the mathematics of conversions, see appendix C.

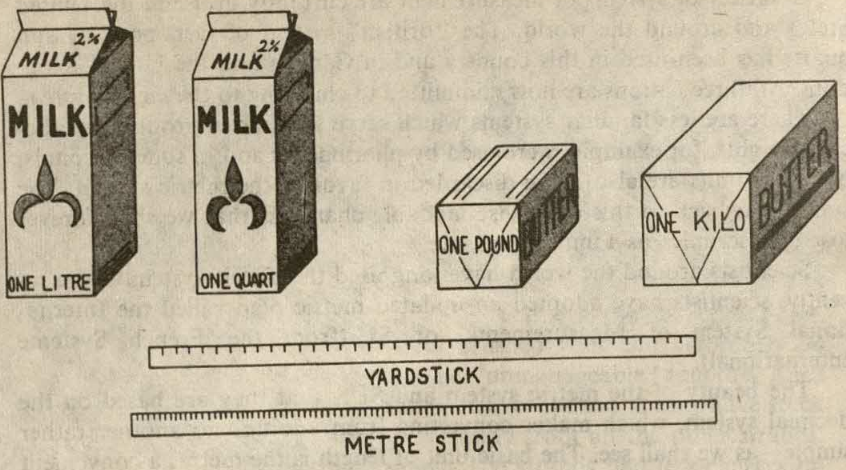

Figure 1.11 A comparison of metric and British units.

Example 1.2 Convert 0.74 mi to feet.

$$0.74\text{ mi} \times \frac{5280\text{ ft}}{1\text{ mi}} = 3907\text{ ft}$$

Example 1.3 Convert 1247 mg to grams.

$$1247\text{ mg} \times \frac{1\text{ g}}{1000\text{ mg}} = 1.247\text{ g}$$

Example 1.4 Convert 12.47 oz to pounds.

$$12.47\text{ oz} \times \frac{1\text{ lb}}{16\text{ oz}} = 0.7794\text{ lb}$$

See? In conversions using British units, you multiply and divide by 36 or 5280 or 12, and so on. In metric conversions, you multiply and divide by 10 or 100 or 1000, and so on. You need only shift the decimal point when doing metric conversions.

To convert from one system to another, you need a list of equivalents such as that on page 9 (or the more extensive list in appendix A).

Example 1.5 How many kilograms are there in 140 lb?

$$140\text{ lb} \times \frac{1\text{ kg}}{2.2\text{ lb}} = 64\text{ kg}$$

Example 1.6 How many metres are there in 764 ft?

$$764\text{ ft} \times \frac{12\text{ in.}}{1\text{ ft}} \times \frac{1\text{ m}}{39.4\text{ in.}} = 233\text{ m}$$

Example 1.7 How would you describe a young man who is 1.6 m tall and weighs 90 kg?

$$1.6\text{ m} \times \frac{39.4\text{ in.}}{1\text{ m}} \times \frac{1\text{ ft}}{12\text{ in.}} = 5.25\text{ ft}$$

$$90\text{ kg} \times \frac{2.2\text{ lb}}{1\text{ kg}} = 198\text{ lb}$$

The young man is 5 ft 3 in. tall and weighs almost 200 lb. Let us be generous and say he is well muscled.

Scientists also use a temperature scale different from that commonly used in local weather reports. The familiar Fahrenheit scale defines the freezing temperature of water as 32 °F and the boiling point as 212 °F. For much of their work, many scientists use the Celsius scale (still referred to as centigrade by some), on which the freezing temperature of water is defined as 0 °C and the boiling point as 100 °C. The scale between these two reference points is divided into 100 equal divisions, each a Celsius degree. Thus, the Celsius degree is larger than the Fahrenheit degree. It requires only 100 of the larger Celsius degrees to cover the same temperature range as do 180 (212 − 32) Fahrenheit degrees.

For conversions from one system to the other, the following equations are used.

$$°\text{F} = \frac{9}{5}°\text{C} + 32$$

$$°\text{C} = \frac{5}{9}(°\text{F} - 32)$$

Example 1.8 The temperature in Tucson reached 113 °F on a summer day. What temperature would that be on the Celsius scale?

$$\frac{5}{9}(113 - 32) = \frac{5}{9}(81) = 45\text{ °C}$$

Example 1.9 If a woman has a temperature of 40 °C, how sick is she?

$$\frac{9}{5}(40) + 32 = 72 + 32 = 104\text{ °F}$$

Pretty sick.

Example 1.10 The temperature at St. Louis dropped to −10 °C on a winter night. What was the temperature on the Fahrenheit scale?

$$\frac{9}{5}(-10) + 32 = -18 + 32 = 14\text{ °F}$$

Example 1.11 It is recommended that the temperature of a food freezer be maintained at 0 °F. What is the temperature on the Celsius scale?

$$\frac{5}{9}(0 - 32) = \frac{5}{9}(-32) = -18\ ^\circ\mathrm{C}$$

The SI unit for temperature is the Kelvin (K). The Kelvin and the Celsius degree are the same size. The Kelvin scale is called an *absolute scale* because its zero point is the coldest temperature possible, or absolute zero. This fact was determined by theoretical considerations and has been confirmed by experiment. The zero point on the Kelvin scale is equal to −273.15 °C. Note that there are no negative temperatures on the absolute scale. To convert from Celsius to Kelvin, you merely add 273.15 to the Celsius temperature.

$$K = {}^\circ C + 273.15$$

Example 1.12 What is the boiling point of water in Kelvin?
The boiling point of water is 100 °C.

$$100 + 273 = 373\ \mathrm{K}$$

Scientists often need to measure amounts of heat energy. You should not confuse heat with temperature. Heat is a measure of quantity, that is, of *how much energy* a sample contains. Temperature is a measure of intensity, that is, of *how energetic* each individual particle of the sample is. A glass of water at 70 °C contains less heat than a bathtub of water at 60 °C. The particles of water in the glass are more energetic, on the average, than those in the tub, but there is far more water in the tub and its total heat content is greater. The SI unit of heat is the *joule* (J), but we will use the more familiar *calorie* (cal).

$$1\ \mathrm{cal} = 4.18\ \mathrm{J}$$

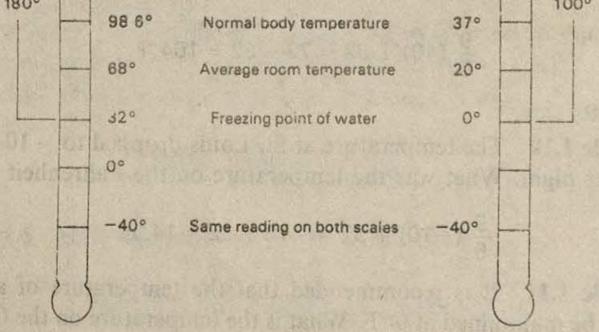

Figure 1.12 A comparison of the Fahrenheit and Celsius temperature scales.

A calorie is the amount of heat required to raise the temperature of 1 g of water 1 °C. There is a more precise definition than this, but for our purposes the simpler version will do.

Example 1.13 How many calories would it take to raise the temperature of 250 g of water from 25 °C to 100 °C?

The definition of *calorie* indicates that 1 cal is required for every degree of change for every gram of water. Thus, the heat capacity of water is

$$\frac{\frac{1\ \text{cal}}{1\ \text{g}}}{1\ ^\circ\text{C}}$$

or

$$\frac{1\ \text{cal}}{(1\ \text{g})(1\ ^\circ\text{C})}$$

The temperature change is 100 °C − 25 °C, or 75 °C, and the amount of water is 250 g.

$$250\ \text{g} \times 75\ ^\circ\text{C} \times \frac{1\ \text{cal}}{(1\ \text{g})(1\ ^\circ\text{C})} = 18\,750\ \text{cal}$$

For the measurement of the energy content of foods, the *large Calorie* (note the capital *C*), or *kilocalorie,* is used. A dieter may be aware that a banana split contains 1500 Cal. If the same dieter realized that that meant 1 500 000 calories, giving up the banana split might be easier.

Example 1.14 If a hot-water bag contains 1 kg of water at 65 °C, how much heat will it have supplied to someone's aching muscles by the time it has cooled to 20 °C?

$$1\ \text{kg} = 1000\ \text{g}$$

$$1000\ \text{g} \times (65 - 20)\ ^\circ\text{C} \times \frac{1\ \text{cal}}{(1\ \text{g})(1\ ^\circ\text{C})} =$$

$$1000\ \text{g} \times 45\ ^\circ\text{C} \times \frac{1\ \text{cal}}{(1\ \text{g})(1\ ^\circ\text{C})} = 45\,000\ \text{cal or } 45\ \text{kcal}$$

1.6 How Dense It Is

An important property of matter, particularly in scientific work, is *density.* When one speaks of lead as "heavy" or aluminum as "light," one is referring to the density of these metals. This term is defined as the amount of mass (or weight) per unit of volume. The equations

$$D = \frac{M}{V}$$

and

$$M = D \times V$$

are useful for making calculations, and density values are usually reported in grams per millilitre (g/ml) or grams per cubic centimetre (g/cm^3).

Example 1.15 What is the density of iron if 156 g of iron occupy a volume of 20 cm^3?

$$\frac{156\ \text{g}}{20\ \text{cm}^3} = 7.8\ \text{g/cm}^3$$

Example 1.16 How much will a litre of gasoline weigh if its density is 0.66 g/ml?

$$0.66\ \text{g/ml} \times 1\ \ell \times \frac{1000\ \text{ml}}{1\ \ell} = 660\ \text{g}$$

The density of water is 1 g/ml, or 1 g/cm^3, or 1 g/cc (remember that 1 ml = 1 cm^3). This nice round number for the density of water is not an accident. The metric system was originally set up in such a way as to ensure that this was the case.

A term related to density is *specific gravity*. Specific gravity is the ratio of the mass of any substance to the mass of an equal volume of water. The specific gravity of water itself, therefore, is 1. Mercury (the silvery liquid in thermometers, not the planet) has a specific gravity of 13.6. That means it has a density 13.6 times as great as water's. The specific gravity of alcohol is 0.8; thus, alcohol is less dense than water. Because it is the ratio of two values, specific gravity is a number without units, whereas density is reported in units of mass per volume. And because, in the metric system, the density of water is 1 g/ml, the specific gravity of a substance is numerically the same as its density.

$$\text{Specific gravity of a substance} = \frac{\text{density of the substance}}{\text{density of water}}$$

Example 1.17 The density of chloroform is 1.5 g/ml. What is its specific gravity?

$$\frac{1.5\ \text{g/ml}}{1.0\ \text{g/ml}} = 1.5$$

Specific gravity is frequently measured by a device called a hydrometer. The hydrometer is placed in the solution whose specific gravity is to be measured. How far it dips down into the liquid is determined by how dense the liquid is (**figure 1.13**). The stem of the hydrometer is calibrated in such a way that the specific gravity can be read directly at the surface of the liquid. Hydrometers can be used to measure "battery acid" in your car, sugar content in maple syrup, dissolved solids in urine, and many other properties of solutions that are related to specific gravity.

Physical measurement, as contrasted to counting, is never exact. One can count exactly 42 people in the classroom, but measurement of the width of a room would give varying results, depending upon the care taken and upon the accuracy of the measuring device.

For those who are interested and those whose work might require it, measurement is discussed more extensively in appendix A, and some conversion tables are provided.

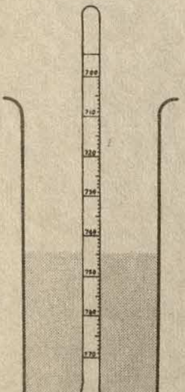

Figure 1.13 A hydrometer. The one shown here measures specific gravities over a range of 0.700 to 0.770.

Problems

1. List three characteristics of science. Are these unique to the scientific discipline?
2. How do scientific models differ from, say, model airplanes or model boats?
3. a. Convert the following to degrees Celsius: 68 °F; 25 °F; −10 °F.
   b. Convert the following to degrees Fahrenheit: −31 °C; 212 °C.
   c. Convert the following to Kelvin: 37 °C; −100 °C.
4. How many metres are there in 50 km? In 25 cm? In 76 ft? In 100 yd?
5. How many decilitres are there in 1 ℓ? In 20 ml? In 15 qt? In 18 gal?
6. How many millilitres are there in 1 cm^3? In 15 cc?
7. How many calories of heat would be required to raise the temperature of 50 g of water from 20 °C to 50 °C?
8. How much heat would be released by 2 kg of water cooling from 90 °C to 20 °C?
9. What is the density of a salt solution if 50 cm^3 of the solution weigh 57 g?
10. A 1-ℓ container of carbon tetrachloride weighs 1.6 kg. What is the density of carbon tetrachloride?
11. What is the weight of 50 ml of mercury? The density of mercury is 13.6 g/ml.
12. If the density of a normal urine sample is 1.02 g/ml, what is its specific gravity?
13. How do gases, liquids, and solids differ in their properties?
14. What is the difference between kinetic energy and potential energy?
15. Explain the difference between mass and weight.
16. Describe what happens to two particles with like charges when they are brought close together. What happens to particles with unlike charges when they are brought close together?
17. Calculate your weight in kilograms. Calculate your height in centimetres.
18. Would you weigh the same on the moon as you do on the earth? Would your mass be the same?

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chapter 2

Atoms

Atom. The word is so familiar that it seems it must always have been with us. Yet the birth of the concept was a difficult one, spanning more than two millennia. It took another century or so for our idea of the atom to mature—and what started as a hard sphere grew to a complicated, fuzzy cloud of matter. In this chapter we will look at the development of the concept of the atom. We will examine the parts from which atoms are made. Then we will consider how the parts may be arranged to make up the hundred-odd kinds of atoms of which the entire universe is made.

Figure 2.1 Democritus. (Duplication courtesy of the Smithsonian Institution, Washington, D.C.)

For all practical purposes, atoms are eternal. We can't get rid of those that we don't want. We can bury them under the ground or throw them into the sea. We can combine them in different ways. Today, we can even do what a 10th-century alchemist could only dream of doing: we can change one kind of atom into another. But they still won't go away. We should keep that in mind when we consider solutions to pollution problems.

A knowledge of the structure of atoms is of utmost importance. Most of the analyses for components of blood and urine—analyses upon which many medical diagnoses are based—depend on a knowledge of the structure of atoms and the way that structure changes when energy is absorbed. Learn all you can about atoms. They are what you and all the universe are made of.

2.1 Greek Atoms

In the fifth century B.C., Leucippus and his pupil Democritus strolled upon an Aegean beach. Leucippus is said to have wondered aloud whether the water of the sea was continuous, as it appeared to be, or whether it might be composed of tiny, separate particles like the grains of sand on the beach. From a distance, the sand appeared continuous, but closer inspection revealed the separate grains. Leucippus could divide the water into drops and each drop into smaller drops. Was there any reason this process could not be continued indefinitely, yielding ever smaller drops of water? This idea of endless divisibility was the prevailing view of the Greek philosophers of that time, but Leucippus, on the basis of intuition alone, concluded that there must be a limit to divisibility—that there must be ultimate particles that could not be further subdivided.

Democritus, who lived from about 470 to 380 B.C., gave these ultimate particles names. He called them *atomos,* meaning "indivisible." Democritus also expanded the theory of matter. He believed that atoms of each element* were distinct in shape and size. Thus, the atoms of water might be smooth, round balls which could easily roll over one another; that would explain why water flowed so readily. The atoms of fire could be sharp-edged, thus causing pain when they touched the hand. Substances other than the elements were considered mixtures of elements. One substance could be changed into another if the proportionate number of atoms of each element could be altered.

This atomic theory was expanded five centuries later by a Roman, Lucretius. In a long poem, *On the Nature of Things,* Lucretius gave strong arguments for the atomic nature of matter. These ancient theories seem remarkably modern in many respects. However, neither Greeks nor Romans had the means to determine which view of matter—as atomistic or as continuous—was correct. In fact the ancients almost never experimented, preferring to reason from what they called "first principles." Therefore, the atomistic theory remained a minority view for 2000 years. It just didn't seem reasonable to most ancient theorists that a piece of matter could be so small that it could not be split into still smaller pieces.

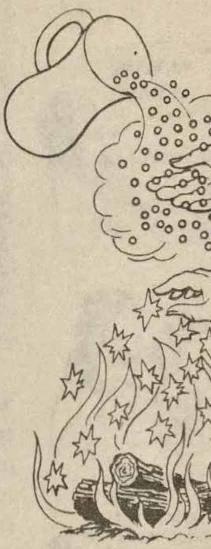

Figure 2.2 Democr
imagined that "atoms
water might be smoo
balls and that "atoms
could have sharp edg

> **"To understand the very large, we must understand the very small."**
>
> **Democritus**

2.2 The French: Experiment and Revolution

By about 1700 A.D., scientists were observing more carefully and measuring more accurately.

Antoine Laurent Lavoisier, a Frenchman (1743–1794), perhaps did more than anyone else to establish chemistry as a quantitative science. He found that when a chemical reaction was carried out in a closed system, the total weight of the system was not changed. Perhaps the most important chemical reaction that Lavoisier performed was the decomposition of the red oxide of mercury to form metallic mercury and a gas which he named oxy-

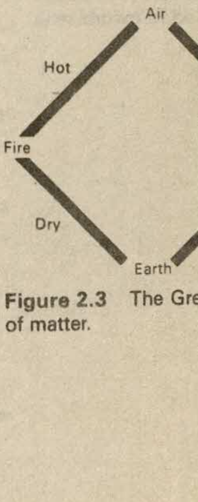

Figure 2.3 The Gre
of matter.

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*Elements were considered basic substances which were not composed of some combination of even more basic substances. The Greeks believed that there were only four elements: earth, air, fire, and water. The relationship between the four elements and the four "principles"—hot, moist, dry, and cold—is shown in **figure 2.3.**

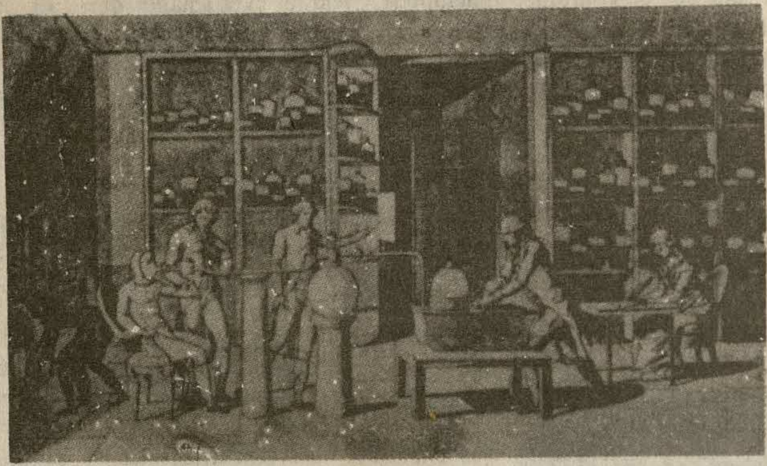

Figure 2.4 Lavoisier in his laboratory. This sketch, adapted from one made by his wife, shows him studying respiration. (Reprinted with permission from Smith, Henry D., *Torchbearers of Chemistry,* New York: Academic Press, 1949. Copyright © 1949 by Academic Press, Inc.)

gen. The reaction had been carried out before—by Karl Wilhelm Scheele, a Swedish apothecary (1742–1786), and by Joseph Priestley, a Unitarian minister who later fled England and settled in America—but Lavoisier was the first to weigh all the substances present before and after the reaction. Lavoisier was also the first to interpret the reaction correctly.

Lavoisier carried out many quantitative experiments. He found that, when coal was burned, it united with oxygen to form carbon dioxide. He also experimented with animals. When a guinea pig breathed, oxygen was consumed and carbon dioxide was formed. Lavoisier therefore concluded that respiration was related to combustion. In each of these reactions he found that matter was conserved.

Lavoisier summarized his findings in these and other experiments by formulating a scientific law.* His *law of conservation of mass* holds that matter is neither created nor destroyed during a chemical change. In other words, if one weighed all the products of a reaction—solids, liquids, and gases—the total would be the same as the weight of all the original substances (called reactants, or starting materials).

Scientists had by this time abandoned the Greek idea of the four elements and were almost universally using Robert Boyle's operational defini-

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*Scientific "laws" merely summarize experimental data. For example, Lavoisier found that in each of the reactions he carried out, the total weight of products was equal to the total weight of reactants. The law of conservation of mass simply summarizes these findings. A modification of this law was made necessary when Albert Einstein pointed out the relationship between matter and energy. We shall consider this modification later. For the moment, we shall work with Lavoisier's law.

One of the earliest illustrations of the law of definite proportions is found in the work of a Swedish chemist, J. J. Berzelius (1779–1848). He heated 10 g of lead with varying amounts of sulfur to form lead sulfide. Since lead is a soft, greyish metal, sulfur is a yellow solid, and lead sulfide is a shiny black solid, it was easy to tell when all the lead had reacted. Excess sulfur was easily washed away by carbon disulfide, a liquid which dissolves sulfur but not lead sulfide. As long as he used at least 1.56 g of sulfur, he got exactly 11.56 g of lead sulfide. Any sulfur in excess of 1.56 g was left over, unreacted. If he used more than 10 g of lead with 1.56 g of sulfur, he got 11.56 g of lead sulfide with lead left over. These reactions are illustrated in **figure 2.7** and explained in **figure 2.10.**

tion, put forth over a century before. Boyle, an Englishman, in his book *The Sceptical Chymist,* published in 1661, said that supposed elements must be tested to see if they really were simple. If a substance could be broken down into simpler substances, it was not an element. The simpler substances might be elements and would be so regarded until such time (if it ever came) as they in turn could be broken down into still simpler substances. On the other hand, two or more elements might combine to form a complex substance, called a *compound.*

Using Boyle's definition, Lavoisier included a table of elements in his book, *Elementary Treatise on Chemistry.* His table listed light and caloric (heat) as elements and included some substances we now know to be compounds. Lavoisier was the first to use modern, somewhat systematic names for the chemical elements. He is often called the "father of chemistry" and his book is regarded as the first chemistry textbook. Incidentally, Lavoisier lost his head (on the guillotine) during the French Revolution, but not because of his chemical research. In those days no one was a full-time chemist. Lavoisier had another job on the side. He was a tax collector for Louis XVI, and it was in this capacity that he incurred the wrath of the French peasantry.

In 1799, Joseph Louis Proust showed that a substance called copper carbonate, whether prepared in the laboratory or obtained from natural sources, contained the same three elements—copper, carbon, and oxygen—and always in the same proportion by weight—5.3 parts of copper to 4 parts of oxygen to 1 part of carbon. To summarize this and numerous other ex-

THAT IS AN ELEMENT!
ZAP!
AS I WAS SAYING, THAT WAS A COMPOUND. THOSE MIGHT BE ELEMENT

Figure 2.5 By t
Lavoisier, scientist
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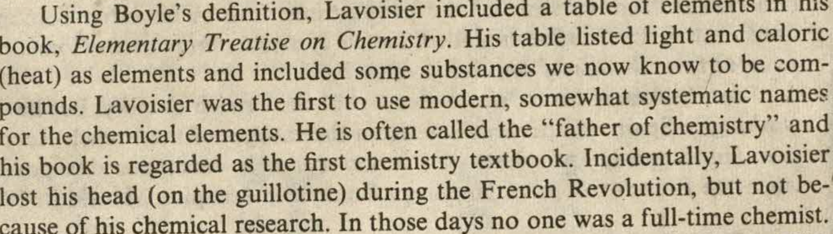

Figure 2.6 Whether synthesized in the laboratory or obtained from various natural sources, copper carbonate always has the same composition. Analysis of this compound led Proust to formulate the law of definite proportions.

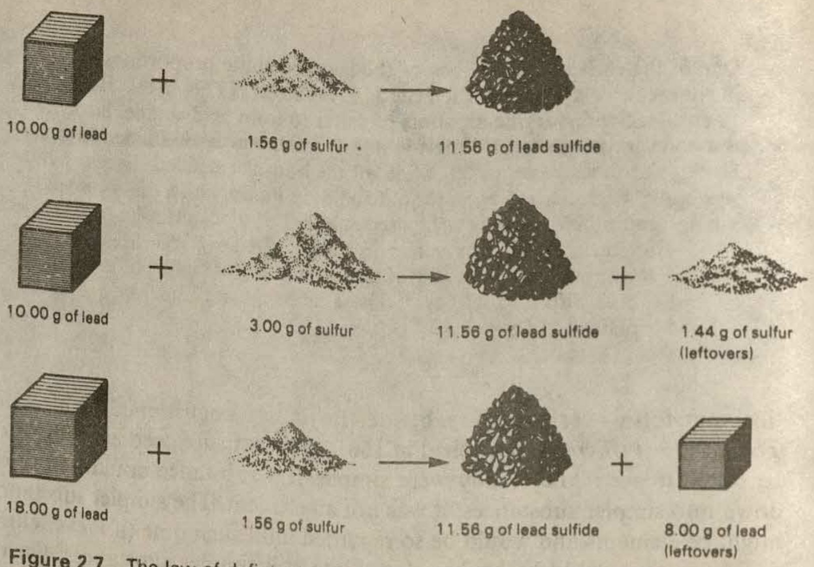

Figure 2.7 The law of definite proportions.

periments, Proust formulated a new law. A compound, he said, always contains elements in certain definite proportions, and in no other combinations. This generalization he called the *law of definite proportions* (sometimes referred to as the *law of constant composition*).

Proust, like Lavoisier, was a member of the French nobility, but he was working in Spain, temporarily safe from the ravages of the French Revolution. His laboratory was destroyed, however, and he was reduced to poverty when the French troops of Napoleon Bonaparte occupied Madrid in 1808.

Figure 2.8 John Dalton. (Duplication courtesy of the Smithsonian Institution, Washington, D.C.)

2.3 English Atoms

Lavoisier's law of conservation of mass and Proust's law of definite proportions were repeatedly confirmed by experiment. This led to attempts to formulate theories that would account for these laws. In science, a *theory* is a model that consistently explains those observations summarized in various laws.

John Dalton, an English school teacher, was one of those who proposed a model to explain the accumulating experimental data. As he developed the details of his model, he uncovered a third "law" which his theory would have to explain. Proust had previously observed that a compound contains elements in certain definite proportions and only those proportions. Dalton's new law stated that elements might combine in more than one set of proportions. If they did, though, each different combination would produce a different compound. For example, carbon combined with oxygen in a weight proportion of 3 parts of the former to 8 parts of the latter to form carbon dioxide, a gas familiar as a product of respiration and of the burning of wood or coal. But Dalton found that 3 parts of carbon would also combine with 4 parts of oxygen by weight to form a poisonous gas that we know

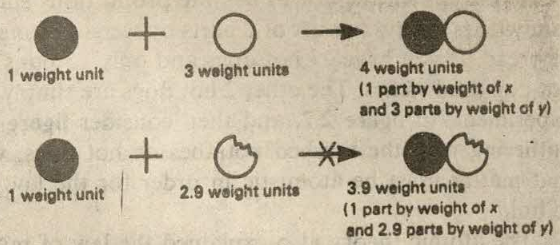

Figure 2.9 According to the atomic theory, only whole atoms may combine. The second scheme is impossible.

today as carbon monoxide. After observing similar multiple combinations for other sets of elements, Dalton put forth his *law of multiple proportions.*

In the same year, he set down the details of his *atomic theory,* a model which offered a logical explanation for the several laws we have mentioned. His reasoning went something like this. If matter is continuous, why should 1 part by weight of x always combine with 3 parts by weight of y? Why shouldn't 1 part of x also combine with 2.9 parts of y? Or 3.1 parts of y? On the other hand, if matter is atomistic, only whole atoms should combine (atoms are, after all, indivisible). If an atom of y weighed three times as much as an atom of x, then the compound formed by the combination of an x and a y would have to consist of 1 part by weight of x and 3 parts by weight of y. An analogy may clarify this point. If you have mashed potatoes and gravy (call them continuous foods), you can have a lot of mashed potatoes and a little bit of gravy, or vice versa. There are no set amounts which go together. On the other hand, if you have a hot dog sandwich (an atomistic food), you need a bun for every hot dog. If the hot dogs weigh twice as much

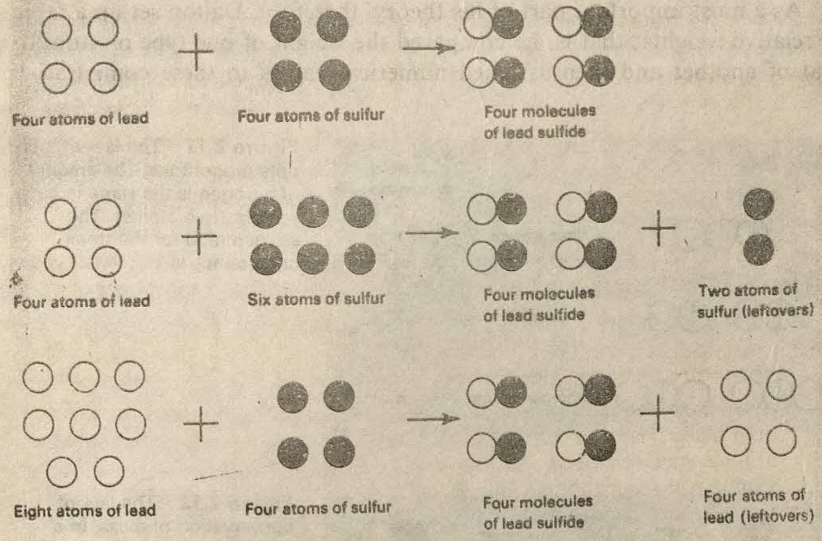
Four atoms of lead
Four atoms of sulfur
Four molecules of lead sulfide
Four atoms of lead
Six atoms of sulfur
Four molecules of lead sulfide
Two atoms of sulfur (leftovers)
Eight atoms of lead
Four atoms of sulfur
Four molecules of lead sulfide
Four atoms of lead (leftovers)

Figure 2.10 The law of definite proportions. Berzelius' experiment interpreted in terms of Dalton's atomic theory.

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as the buns, then the law of definite proportions simply notes that hot dog sandwiches always consist of 2 parts by weight of meat and 1 part by weight of bread. If you have 27 hot dogs and only 25 buns, you can only make 25 hot dog sandwiches. The other 2 hot dogs are simply left over (see Berzelius' experiment, in **figure 2.7,** and then consider **figure 2.10**). Dalton (without bothering with the mashed potatoes or hot dogs, we presume) concluded that matter must be atomistic in order for the law of definite proportions to hold.

The atomic theory also explained the law of multiple proportions. The difference between carbon dioxide and carbon monoxide is that, in the former compound, one atom of carbon always combines with two atoms of oxygen and, in the latter, one atom of carbon always combines with only one atom of oxygen. **Figure 2.11** shows how oxygen and nitrogen combine.

Finally, the law of conservation of mass can also be understood in terms of the atomic theory. When a reaction occurs and the reactants change to products, this change simply involves a reordering of atoms. Matter is neither lost nor gained; it is simply rearranged (**figure 2.12**).

An atomistic view of nature was not unique to Dalton. We have noted that the term *atom* was coined by a Greek who lived in the fifth century B.C. What makes Dalton's atomic theory such an important milestone in the history of chemistry is its emphasis on the weight of atoms. It was an atom's weight (not its shape, as Democritus speculated) that distinguished it from atoms of other elements. All atoms of the element oxygen had identical weights and all atoms of carbon had identical weights, according to Dalton. The weight of the oxygen atom, however, was different from that of the carbon atom. It was precisely this difference in atom weights that accounted for different elements.

As a most important part of his theory, therefore, Dalton set up a table of relative weights; that is, he compared the weight of one type of atom to that of another and then assigned numerical values to these comparative

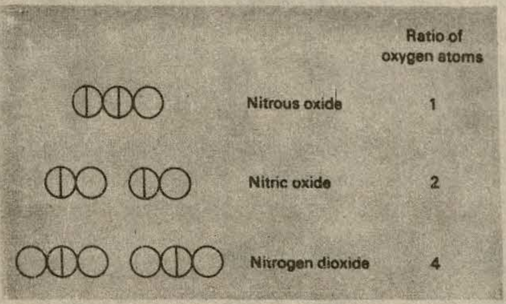


Figure 2.11 The law of multiple proportions. The amount of nitrogen is the same in each sample (two atoms). The oxygen ratio for the three compounds is 1 : 2 : 4.

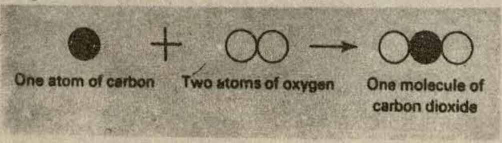
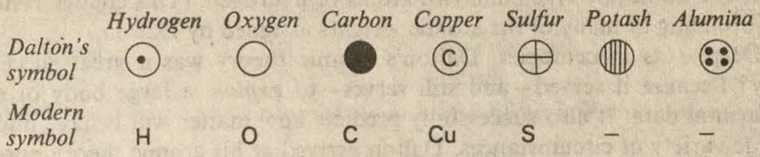
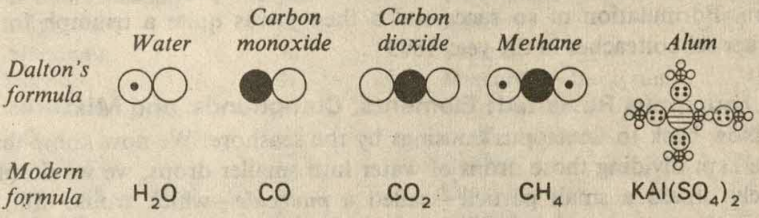


Figure 2.12 The law of conservation of mass. In a chemical reaction, atoms are merely rearranged (not created nor destroyed); thus, matter is conserved.

John Dalton also invented a set of symbols to represent the different kinds of elements.



He used these in combination to represent chemical compounds.



Notice that some of Dalton's formulas were incorrect and that his symbolism was quite cumbersome. It was soon replaced by the modern symbols of one or two letters. Berzelius introduced the modern symbolism, about which Dalton, who had apparently forgotten his structure for alum, commented: "Berzelius' symbols are horrifying. A young student might as soon learn Hebrew as make himself acquainted with them."

weights.* The lightest atom he found was hydrogen, so he assigned a value of 1 to the weight of the hydrogen atom. His studies convinced him that carbon atoms weighed six times as much and oxygen atoms eight times as much as hydrogen. These atoms were, therefore, assigned values of 6 and 8. Thus, carbon monoxide was made up of one atom of carbon combined with one atom of oxygen to give a weight ratio of 6 parts of carbon to 8 of oxygen (or 3 to 4). Carbon dioxide was made up of one atom of carbon combined with two atoms of oxygen to give a weight ratio of 6 parts of carbon to 16 parts of oxygen (or 3 to 8). Methane, according to Dalton, was made up of one atom of carbon and two atoms of hydrogen, giving a weight ratio of 6 parts of carbon to 2 parts of hydrogen (or 3 to 1). We now know that methane has one atom of carbon and four atoms of hydrogen. In fact, many of the entries in Dalton's table of atomic weights were wrong,

Figure 2.13 Jöns Jak
Berzelius, a Swedish che
invented modern chemic
symbols. (Reprinted witl
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*Atoms are extremely minute. In the 19th century, it was impossible to determine actual weights of atoms. Indirect measurements, however, could indicate their relative weights. These relative weights are usually expressed in terms of atomic mass units (amu). This unit of weight (mass) was simply invented for atoms and molecules. Hydrogen weighs 1 amu. Since oxygen weighs 16 times as much as hydrogen (as opposed to Dalton's incorrectly assigned value of 8), its weight is 16 amu.

mainly because he assumed water to be made up of one atom of oxygen combined with one atom of hydrogen. We know today that water is made up of one atom of oxygen and two atoms of hydrogen. (This change results in a doubling of many of the atomic weights assigned by Dalton.)

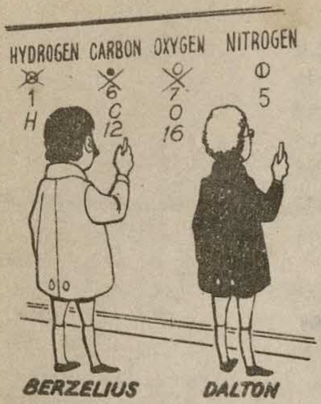

Figure 2.14 Berzelius corrected some of Dalton's atomic weights as well as modernizing Dalton's chemical symbols.

Despite its inaccuracies, Dalton's atomic theory was a great success. Why? Because it served—and still serves—to *explain* a large body of experimental data. It also successfully predicts how matter will behave under a wide variety of circumstances. Dalton arrived at his atomic theory purely on the basis of reasoning power, and with modest modification it has stood the test of time and the assault of modern, highly sophisticated instrumentation. Formulation of so successful a theory was quite a triumph for a Quaker schoolteacher in the year 1803!

2.4 Leucippus Revisited: Elements, Compounds, and Mixtures

Now back to Leucippus' musings by the seashore. We now know that, if we kept dividing those drops of water into smaller drops, we would ultimately obtain a small particle—called a *molecule*—which would still be water. If we divided that particle still further, we would obtain two atoms of hydrogen and one atom of oxygen. And if we divided those. . . . But that's a story for another time. Dalton regarded the atom as indivisible.

We define an *element* in terms of the atoms of which it is composed. In an element, all the atoms are of the same kind. Dalton would have said that "the same kind" meant "the same weight." However, this is one aspect of the atomic theory which had to be revised slightly. We will consider precisely what "the same kind" means a bit later in this chapter.

An element and the atoms of the element are represented by a symbol. There are over a hundred elements known today, each represented by a symbol of one or two letters derived from the name of the element (or, sometimes, the Latin name of the element). The first letter of the symbol is always capital; the second is always lowercase. (It does make a difference. For example, Hf is the symbol for hafnium, an element; HF is the formula for hydrogen fluoride, a compound. Similarly, Co is cobalt, an element; CO is carbon monoxide, a compound. More about compounds shortly.) Symbols for a few of the more important elements are given in **table 2.1.**

A *compound* is made up of two or more elements, *always in fixed proportions*. For example, when the compound water is broken down, it is always found to be composed of 89% oxygen by weight and 11% hydrogen by weight. Water is made up of molecules which contain two hydrogen atoms and one oxygen atom. Each hydrogen atom weighs 1, and each oxygen, 16.

Two hydrogens weigh	2
One oxygen weighs	16
Water weighs	18

$$\text{Percentage of hydrogen in water} = \frac{2}{18} \times 100 = 11\%$$

$$\text{Percentage of oxygen in water} = \frac{16}{18} \times 100 = 89\%$$

Table 2.1
Some elements and their symbols

Element	*Symbol*	*Element*	*Symbol*
Hydrogen	H	Iron (ferrum)	Fe
Helium	He	Cobalt	Co
Carbon	C	Copper (cuprum)	Cu
Nitrogen	N	Zinc	Zn
Oxygen	O	Bromine	Br
Fluorine	F	Silver (argentum)	Ag
Sodium (natrium)	Na	Tin (stannum)	Sn
Magnesium	Mg	Iodine	I
Aluminum	Al	Barium	Ba
Silicon	Si	Mercury (hydrargyrum)	Hg
Phosphorus	P	Gold (aurum)	Au
Sulfur	S	Lead (plumbum)	Pb
Chlorine	Cl	Radium	Ra
Potassium (kalium)	K	Uranium	U
Calcium	Ca	Plutonium	Pu

Any size sample of water will be 89% (or $\frac{16}{18}$) oxygen and 11% (or $\frac{2}{18}$) hydrogen.

Example 2.1 How many grams of oxygen are there in 100 g of water?

$$100 \text{ g of water} \times 0.89 = 89 \text{ g of oxygen}$$

or

$$100 \text{ g of water} \times \frac{16 \text{ g of oxygen}}{18 \text{ g of water}} = 89 \text{ g of oxygen}$$

Example 2.2 How many pounds of hydrogen are there in 36 lb of water?

$$36 \text{ lb of water} \times 0.11 = 4 \text{ lb of hydrogen}$$

or

$$36 \text{ lb of water} \times \frac{2 \text{ lb of hydrogen}}{18 \text{ lb of water}} = 4 \text{ lb of hydrogen}$$

Example 2.3 How much water could be made from 32 g of oxygen?

$$32 \text{ g of oxygen} \times \frac{18 \text{ g of water}}{16 \text{ g of oxygen}} = 36 \text{ g of water}$$

Example 2.4 If the compound sulfur trioxide has a weight ratio of 2 parts of sulfur to 3 parts of oxygen, how much oxygen is there in 45 g of sulfur trioxide?

Out of a total of 5 parts (3 + 2) of sulfur trioxide, $\frac{2}{5}$ is sulfur and $\frac{3}{5}$ is oxygen. Therefore,

$$45\text{ g of sulfur trioxide} \times \frac{3\text{ g of oxygen}}{5\text{ g of sulfur trioxide}} = 27\text{ g of oxygen}$$

The law of definite proportions distinguishes compounds from *mixtures.* One can *mix* lead with sulfur in any proportions. However, if sulfur and lead are heated together, they form a compound, lead sulfide, in which the elements are always found in the same definite proportions (87% lead, 13% sulfur). Any extra lead or sulfur is simply left over, unreacted (see **figure 2.7**).

Matter is characterized by its properties. This simply means that we know we have water and not, say, gasoline because water has certain characteristics or properties which distinguish it from gasoline. For example, it is very hard to start a fire by dousing something with water and then lighting it with a match. *Chemical properties* describe how one substance reacts with other substances; to demonstrate a chemical property, a substance must undergo a change in composition. *Physical properties* involve no change in composition. Such characteristics as color, hardness, density, and melting point are physical properties. Some physical properties of sulfur, for example, are that it is a brittle yellow solid with a density of 2.07 g/cm^3 at room temperature. If you perform an experiment to determine the density of sulfur, you will still have sulfur when you are finished. Some chemical properties of sulfur are that it reacts with oxygen, with carbon, and with iron. These reactions yield, in turn, sulfur dioxide, carbon disulfide, and iron sulfide—all new substances.

2.5 The 19th-Century Atom

Dalton, who set forth his atomic theory in 1803, regarded the atom as hard and indivisible. It wasn't long, however, before that simple picture underwent significant modification. Indeed, even a few years prior to the publication of Dalton's theory, evidence which suggested a more complicated structure began to accumulate. In 1800, two English chemists, William

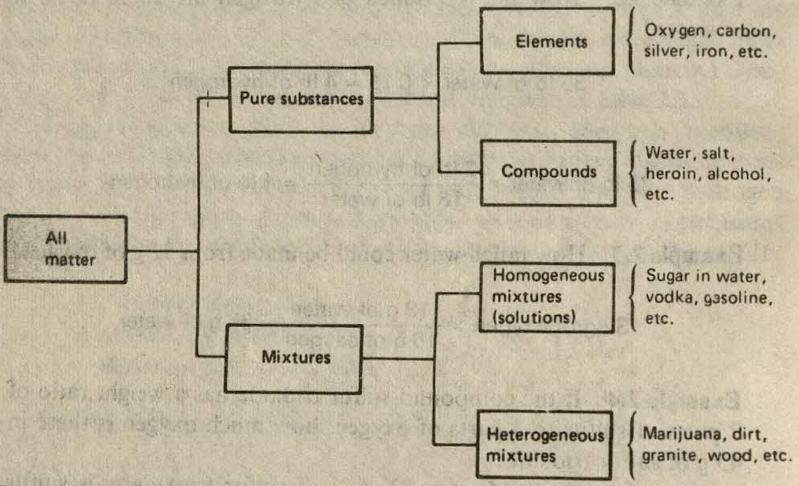
Elements
Oxygen, carbon, silver, iron, etc.
Pure substances
Compounds
Water, salt, heroin, alcohol, etc.
All matter
Homogeneous mixtures (solutions)
Sugar in water, vodka, gasoline, etc.
Mixtures
Heterogeneous mixtures
Marijuana, dirt, granite, wood, etc.

Figure 2.15 A scheme for classifying matter.

Nicholson and Anthony Carlisle, using the recently invented electric battery, passed an electric current through water and decomposed it into hydrogen and oxygen. Clearly matter could somehow interact with electricity (as the existence of the battery itself indicated). Dalton's model of the atom failed to show how. Evidence of the electrical nature of the atom poured out of 19th-century laboratories, particularly that of the English scientist Michael Faraday. Each new experiment provided information about the structure of atoms. There was, in fact, so much data that we shall limit ourselves to a consideration of just a few critical experiments.

Of major significance was the experimental work of William Crookes and Joseph John Thomson. In 1875, Crookes carried out studies in an evacuated glass tube. Into the tube were inserted two metal disks which were connected to a source of electric current. The two disks were called *electrodes,* and when the system was connected to the voltage source, one disk became positively charged and the other became negatively charged. The positive electrode was called the *anode;* the negative one, the *cathode.* Crookes' tube was designed so that the air could be removed from it and the interior maintained under a vacuum. When this was done, a beam of current passed from the cathode to the anode in a straight line through the vacuum. The beam was termed a *cathode ray* (**figure 2.19**).

But just what were these cathode rays? Streams of particles, the British scientists stoutly maintained. No, they were much more likely to be a form of light, made up of waves, the Germans insisted. Who was right? The answer in such cases comes—at least should come—from experimentation, not politics. It was J. J. Thomson who provided the answer in 1897. He showed that the cathode rays were deflected in an electric field. To one side of the Crookes tube was placed a metal plate which carried a positive charge, and to the opposite side was placed a plate with a negative charge. As the ray traveled from the cathode to the anode, it was attracted by the positive plate and repelled by the negative plate (**figure 2.20**). Thus, the rays must be composed of negatively charged *particles.* (It was known that light waves were not deflected by electric fields.) The name *electron* was given to those negatively charged particles. Thomson was also able to measure the mass-to-charge ratio of the cathode-ray particle by determining the amount of deflection in a magnetic field of known strength. A more massive particle with a charge is not deflected as much as a smaller particle with the same charge is. He couldn't measure either the mass or charge separately, though. This situation is similar to a person's being able to determine that an apple weighs a thousand times as much as an apple seed but not knowing the weight in grams of the apple or its seed. For his work, Thomson won the Nobel Prize in physics in 1906. (Thomson's son, George Paget Thomson, also won a Nobel Prize for his studies of electrons.)

The properties of the cathode ray were the same regardless of the material from which the cathode was made. Cathodes made from different elements emitted streams of particles with identical mass and charge. Thus, electrons came to be regarded as constituents of all matter. Note that Dalton's model of the atom could not account for these experimental results.

Figure 2.16 Michael F
day, a British scientist w
helped prove that matter
electrical in nature. (Rep
with permission from Sm
Henry D., *Torchbearers c*
Chemistry, New York: Ac
Press, 1949. Copyright ©
by Academic Press, Inc.)

Figure 2.17 Sir Williar
Crookes, a British scienti
invented the cathode-ray
(Reprinted with permissi
from Weeks, Mary E.,
Discovery of the Element
Easton, Pa.: Chemical Ed
tion Publishing, 1968.
Copyright © 1968 by th
Chemical Education Pub
Company.)

Figure 2.18 J. J. Thomson, a British scientist who determined the mass-to-charge ratio of the electron. (Reprinted from Thomson, George, *The Electron,* Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1972.)

According to him, different elements had different atoms and these atoms were indestructible. There was no way for streams of identical particles to come from Daltonian atoms of different elements.

In 1886, a German scientist named Eugen Goldstein conducted some experiments in equipment similar to Crookes'. Goldstein, however, worked with small amounts of various gases in the tube and used a cathode disk which had perforations in it (**figure 2.21**). He found that, at the same time that rays consisting of electrons left the cathode and sped off toward the anode, positive rays were also formed within his tube and were attracted toward the cathode. These positive rays, as they raced toward the cathode, passed through the holes in the cathode and eventually struck the end of the tube, causing it to glow. It was not until 1907, however, that a study of the deflection of these particles in a magnetic field revealed that, unlike the

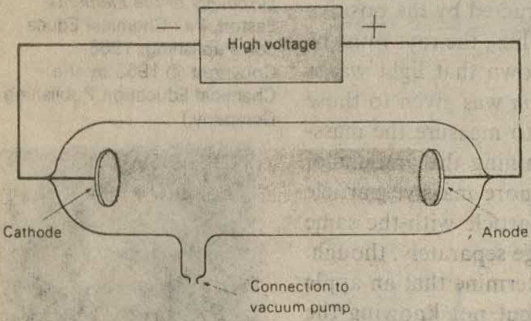

Figure 2.19 A simple gas discharge tube.

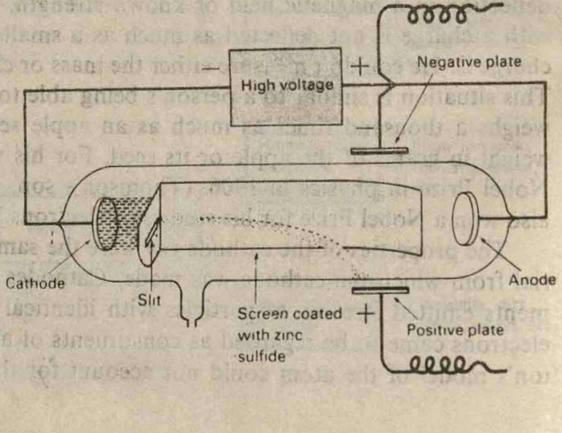

Figure 2.20 Thomson's apparatus showing deflection of an electron beam in an electric field. The screen is coated with zinc sulfide, a substance which glows when struck by electrons.

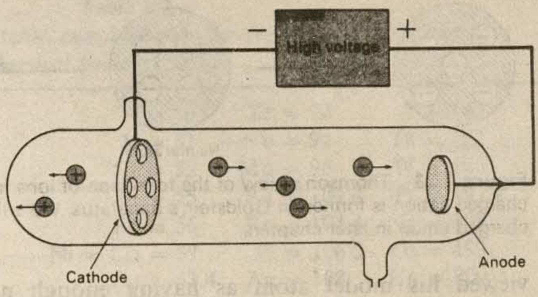

Figure 2.21 Goldstein's apparatus for study of positive particles.

cathode-ray particles, the positive particles were of varying masses. And the masses of these particles varied according to the gas in the tube. Thus, if helium gas was in the tube, the positive ray particles weighed a certain amount. If the gas was hydrogen, the particles weighed a different amount. Hydrogen provided the lightest of all the positive particles, and this lightest positive particle was given a special name, the *proton*. Protons were ultimately found to be 1837 times as massive as electrons. The charges on the proton and the electron were the same size (though opposite in sign), but one particle was many times heavier than the other.

In 1909, an absolute value for the amount of charge carried by an electron was determined by an American, Robert A. Millikan, whose method we shall not detail here. As soon as the size of the electron's charge was determined, it was possible, using Thomson's value for the mass-to-charge ratio, to calculate the mass of the electron. Electrons, it turns out, are extremely light particles, having a mass of only 9.1×10^{-28} g, or 0.000 000 000 000 000 000 000 000 000 91 g. (If you do not understand numbers like 9.1×10^{-28}, you will find out about them in appendix B.)

Since Dalton's picture of the atom was incapable of explaining where all of these particles, both positive and negative, were coming from, J. J. Thomson proposed a new model for the atom (**figure 2.22**). An atom, he suggested, was a solid sphere of positively charged material with negatively charged electrons stuck to it like raisins in a pudding.

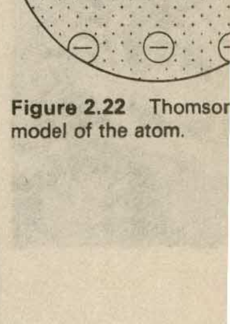

Figure 2.22 Thomson model of the atom.

How did this model explain the work of Crookes, Goldstein, and Thomson himself? Well, the cathode ray was pictured as consisting of electrons which were forcibly knocked out of the atoms of the element making up the cathode when the tube discharged. Since the electron "raisins" of all elements were identical, it did not matter what the cathode was made from. Once the electrons were knocked loose by the high voltage impressed on the tube, they raced across the tube to the positively charged anode.

If a gas was present in the tube when it discharged (Goldstein's experiment), the atoms of the gas would get in the way of the stream of electrons. The electrons of the cathode ray would bang into the gas atoms, knocking some of the electrons in the gas atoms loose (**figure 2.23**). These loosened electrons would simply join the cathode-ray electrons in their flight toward the anode. The gas atom which had just suffered the loss of one of its own electrons, however, would now have an excess of positive charge. Thomson

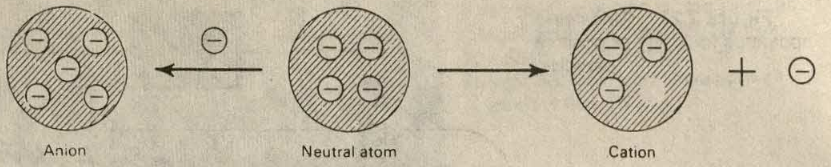

Figure 2.23 Thomson's view of the formation of ions from neutral atoms. The positively charged cation is formed in Goldstein's apparatus. We will consider the negatively charged anion in later chapters.

viewed his model atom as having enough negatively charged electron "raisins" to precisely balance the positive charge on the "pudding." If one of the raisins was lost, then some of the positive charge in the pudding was no longer balanced. These positively charged remnants of the gas atoms would be attracted toward the negatively charged cathode, some of them overshooting their mark and sailing through the perforations in Goldstein's cathode to strike the wall of the tube. Positively charged atoms are called *cations*. Negatively charged atoms, which could be formed by the forcing of extra electrons on an atom, are called *anions*. (We will deal with the formation of anions in later chapters.) A more general term for any charged atom is *ion*. Since the positive ions formed in the discharge tube are simply atoms of the gas in the tube minus an electron, one can see why positive ions from different gases have different masses. Dalton's atomic theory is still correct in picturing atoms of different elements as having different masses. The ions formed when hydrogen is in the tube are the lightest of the cations because hydrogen is the lightest atom.

Figure 2.24 Dmitri Mendeléev, a Russian chemist who invented the periodic table of the elements. (Reprinted with permission from Weeks, Mary E., *Discovery of the Elements*, Easton, Pa.: Chemical Education Publishing, 1968. Copyright © 1968 by the Chemical Education Publishing Company.)

Despite the fact that Thomson's model served quite well to explain the gas discharge tube experiments, it soon fell victim to startling new developments in a new century.

2.6 Out of Chaos: Order in the Universe

Before moving on to the new century, let us take a look at a remarkable development in chemistry which paralleled those described above.

New elements were discovered with surprising frequency. By 1830 there were 55 known elements, all with seemingly different properties and with no apparent order in these properties. Several attempts were made to arrange the elements in some sort of systematic fashion. The most successful arrangement was that of Dmitri Ivanovich Mendeléev (1834–1907), a Russian chemist. He published a *periodic table* of the elements in 1869. His table (**table 2.2**) has the elements arranged, primarily, in order of increasing atomic weight, although in a few cases he placed a slightly heavier element before a lighter one. He did this to get elements with similar chemical properties in the same row. For example, he placed tellurium (which has an atomic weight of 128) ahead of iodine (which has an atomic weight of 127) because the former resembled sulfur and selenium in its properties, whereas the latter was similar to chlorine and bromine.

Mendeléev left a number of gaps in his table. Instead of looking upon those blank spaces as defects, he boldly predicted the existence of elements

Table 2.2
Mendeléev's periodic table, as published in the *Journal of the Russian Chemical Society* (1869)

			Ti = 50	Zr = 90	? = 180
			V = 51	Nb = 94	Ta = 182
			Cr = 52	Mo = 96	W = 186
			Mn = 55	Rh = 104.4	Pt = 197.4
			Fe = 56	Ru = 104.4	Ir = 198
			Ni = Co = 59	Pl = 106.5	Os = 199
H = 1			Cu = 63.4	Ag = 108	Hg = 200
	Be = 9.4	Mg = 24	Zn = 65.2	Cd = 112	
	B = 11	Al = 27.4	? = 68	Ur = 116	Au = 197?
	C = 12	Si = 28	? = 70	Sn = 118	
	N = 14	P = 31	As = 75	Sb = 122	Bi = 210
	O = 16	S = 32	Se = 79.4	Te = 128?	
	F = 19	Cl = 35.5	Br = 80	I = 127	
Li = 7	Na = 23	K = 39	Rb = 85.4	Cs = 138	Tl = 204
		Ca = 40	Sr = 87.4	Ba = 137	Pb = 207?
		? = 45	Ce = 92		
		?Er = 56	La = 94		
		?Yt = 60	Di = 95		
		?In = 75.6	Th = 118?		

as yet undiscovered. Furthermore, he even predicted the properties of some of these missing elements.

In succeeding years many of the gaps were filled in by the discovery of new elements. The properties were often quite close to those Mendeléev had predicted. It was the predictive value of this great innovation that led to the wide acceptance of Mendeléev's chart.

The modern periodic chart (on the inside front cover of this book) now contains more than a hundred elements rearranged so that chemically similar elements are in the same column rather than in the same row. (Essentially, this rearrangement means that Mendeléev's version was just turned on its side.) Chemists still use it to predict the properties of new elements.* The modern version is also a storehouse of information about the various elements. We shall explore the table's potential in this regard shortly.

2.7 Serendipity in Science

Let us now return to the structure of the atom. Many scientific discoveries are described as happy accidents. Something unexpected happens and, as a result, whole new areas of study are opened. Such accidents are of no value unless they happen to a trained observer who can grasp their significance. It is the combination of the right scientist and the right accident that qualifies an event as a case of scientific serendipity.

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*In 1971, a team of six British scientists claimed to have produced element number 112. They confidently placed it in Group IIB, just below mercury (Hg, element number 80), because its properties resembled those of mercury, even though intervening elements had not been discovered. This claim has not been verified by other investigators; thus, it is not accepted by the world community of scientists.

Two such happy accidents occurred in the waning years of the 19th century. In 1895 a German scientist, Wilhelm Konrad Roentgen, was working in a darkroom, studying certain substances which glowed while exposed to cathode rays. To his surprise, he noted this glow in a chemically treated piece of paper held some distance from the cathode-ray tube. The paper even glowed if the tube was located in the next room. Roentgen had discovered a new type of ray, one which could travel through walls! The rays were given off from the *anode* whenever the cathode-ray tube was operating. With seeming lack of imagination, Roentgen called the mysterious, penetrating rays *X rays*. X rays are related to light, unlike cathode rays, which are streams of charged particles.

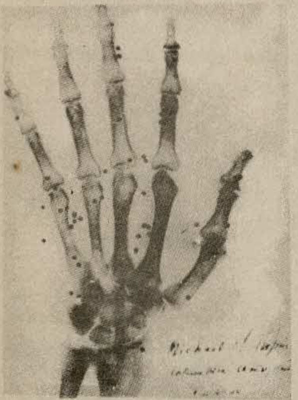

Figure 2.25 An early example of the use of X rays in medicine. Professor Michael Pupin, of Columbia University, made this X ray in 1896 to aid in the removal by surgery of gunshot pellets (dark spots) from the hand of a patient. (Courtesy of Burndy Library, Norwalk, Conn.)

As is often the case when an exciting new discovery is made, many other scientists began to study the new phenomenon.* One, Antoine Henri Becquerel, a Frenchman, had been studying fluorescence, a phenomenon in which certain chemicals, when exposed to strong sunlight, continued to glow even when taken into a dark room. Was this phenomenon related to X rays? he wondered. Becquerel wrapped photographic film in black paper, placed a few crystals of the fluorescing chemical on top of the paper, and then placed it in strong sunlight. He reasoned that, if the glow were ordinary light, it would not pass through the black paper. If, on the other hand, the glow were similar to X rays, it would pass through the black paper and fog the film.

Before Becquerel's studies of fluorescence had progressed very far, he made an important discovery. He was testing a crystal of uranium compound. After being placed in sunlight, it fogged the covered photographic film, suggesting that here, perhaps, was a compound which emitted X rays when it fluoresced. During several cloudy days when work in sunlight was impossible, Becquerel prepared samples and placed them in a drawer. To

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*Chemists and physicists aren't the only ones who jump on bandwagons. The medical community immediately recognized the significance of the penetrating X rays. The X-ray picture shown in **figure 2.25** was taken in February 1896, within two months of the publication of Roentgen's discovery. The round black dots are gunshot pellets whose positions were established for removal by surgery through this picture.

Unfortunately, details of the X-ray apparatus and commercial versions of the equipment were readily available to the public, who were as fascinated by the phenomenon as were scientists. (Roentgen himself would not patent his discovery and, thus, refused to reap its commercial rewards.) While X rays made major contributions to medicine and to basic science, their indiscriminate use by people (including many scientists and physicians) resulted in a number of cases of severe burns and some deaths. It took some time to fully appreciate that rays which could pass through the body could also inflict biological damage as they made their way through.

his great surprise, the photographic film was exposed even though the uranium compound had not been exposed to sunlight. Further experiments showed that, in fact, this radiation had no connection with fluorescence but was a characteristic of the element uranium.

As happened with the discovery of X rays, many other scientists began to study this new type of radiation. One, Marie Sklodowska Curie, gave this new phenomenon the name *radioactivity*. Marie Sklodowska was born in Poland in 1867. She came to Paris to work for her doctor's degree in mathematics and physics. There she met and married Pierre Curie, a French physicist of some note. She, often with the help of her husband, discovered a number of new radioactive elements, including radium. Pierre Curie was killed in a traffic accident 3 years after he, Marie, and Becquerel were awarded the 1903 Nobel Prize in physics. Marie Curie continued to work with radioactivity, winning a second Nobel Prize (for chemistry) in 1911. She died in 1934 of pernicious anemia, perhaps brought on by deprivation, hard work, and long exposure to radiation from the materials she had studied. Her daughter Irène Joliot-Curie and Irène's husband, Frédéric, also won a Nobel Prize for work with radioactive materials. All in all, a remarkable family.

Figure 2.26 Marie Curie i
laboratory. (Culver Pictures

2.8 A New Atom for a New Century

It was soon realized that the radiation emanating from uranium, radium, and other radioactive elements was of three types. When this radiation was passed through a strong magnetic field, one portion was deflected in one direction, another portion was deflected in the opposite direction, and a third was not deflected at all. These portions were named *alpha* (α), *beta* (β), and *gamma* (γ) rays, respectively, by Ernest Rutherford, a New Zealander working at McGill University, in Montreal. The alpha rays were shown to have a mass four times that of the hydrogen atom and a positive

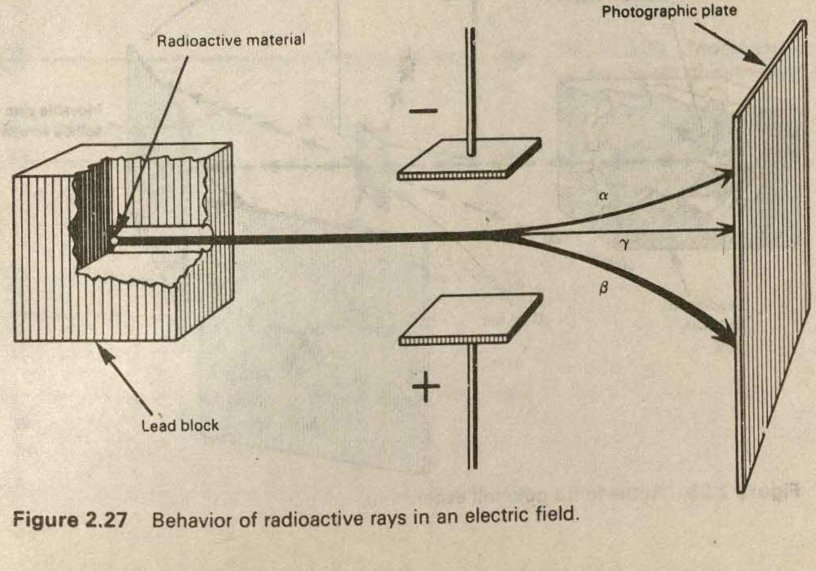


Figure 2.27 Behavior of radioactive rays in an electric field.

Table 2.3
Types of radioactivity

Name	*Symbol*	*Mass (in atomic mass units)*	*Charge*
Alpha	α	4	2+
Beta	β	$\frac{1}{1837}$	1−
Gamma	γ	0	0

charge twice that of the proton (or twice the magnitude of the electron's negative charge). Beta rays were shown to be identical to cathode rays; that is, they were streams of electrons. The charge on an electron or beta particle is assigned a value of 1−. Therefore, the charge on an alpha particle is 2+. Gamma rays were shown to be very much like X rays but even more penetrating. Gamma rays have no mass and no charge. These properties are summarized in **table 2.3.**

Rutherford soon used the positively charged alpha particles to make an important discovery. He placed some highly radioactive material in a lead-lined box that had a tiny hole. Most of the alpha particles emitted by the material in the box were absorbed by the lead, but those escaping through the hole formed a narrow stream of very high energy particles. This apparatus, then, could be aimed like a gun at some "target" (**figure 2.28**).

One target that Rutherford selected was a thin piece of gold foil. With J. J. Thomson's model of the atom in mind, Rutherford expected most of the positively charged alpha particles to be deflected only slightly by the positive charges in the atoms of the gold foil. (Recall that Thomson's "raisin pudding" model had the positive charge spread throughout the atom.) What Rutherford found was that most of the alpha particles went through the foil, which was about two thousand atoms thick, without being deflected

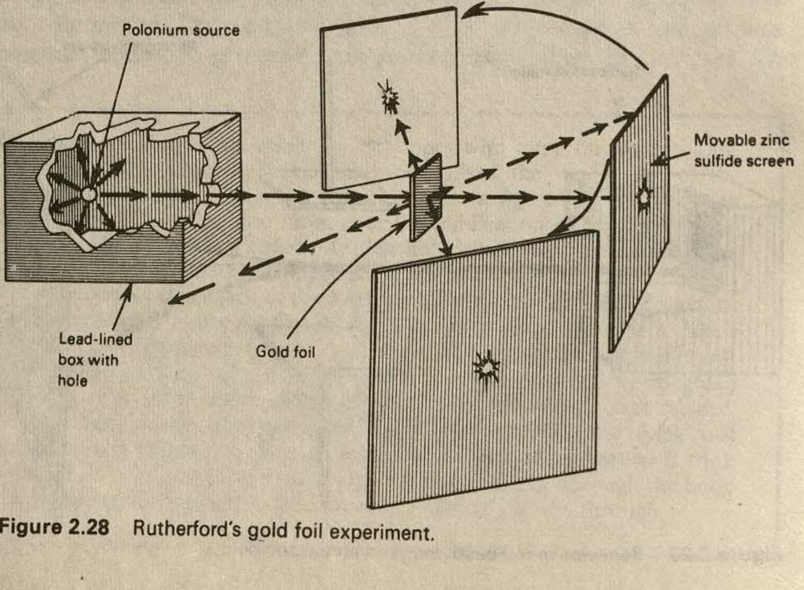


Figure 2.28 Rutherford's gold foil experiment.

at all. This result is understandable if one assumes that the positive portion of the "raisin pudding" atom is really something like pudding in consistency, rather thinly spread and no match at all for a high-energy alpha bullet. The tiny electrons in the atom would not be expected to stop the much more massive alpha particle either. What really amazed Rutherford was the fact that a few of the particles were deflected very sharply, some even bouncing back in the same direction from which they came. This could not be explained with Thomson's model. Either the pudding was soft and let the alpha particles through, or it was hard and bounced them back—but not both.

On the basis of these results Rutherford proposed a new arrangement of the positive and negative parts of the atom. To account for the very strong deflections of some of the alpha particles, he pictured all the positive charge and almost all of the mass concentrated in a very small space. When an alpha particle approached this concentrated, positively charged matter (called the *nucleus* of the atom), it was strongly repelled and, thus, strongly deflected. Since very few alpha particles were deflected, Rutherford concluded that the nucleus must occupy only a fraction of the total volume of the atom. Most of the particles passed right through the atom, because most of the atom was empty space. But this space was not completely empty: it was here that Rutherford placed the negatively charged electrons. He concluded that electrons were so small that their presence in no way interfered with the passage of the alpha particle through the atom, a situation analagous to that of a mouse trying to stop the charge of an enraged bull elephant. Rutherford's nuclear theory of the atom, set forth in 1911, was revolutionary indeed. He postulated that all the positive charge and virtually all the mass were concentrated in the tiny, tiny nucleus. The negatively charged electrons, he said, had virtually no mass yet occupied nearly all the volume of the atom. Thomson's raisin pudding was replaced by a model which can be pictured as follows: a BB (the nucleus) in the middle of a volume of space

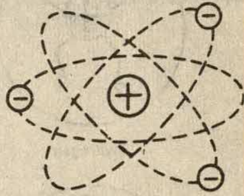


Figure 2.29 Rutherford viewed the atom as a posi charged nucleus surround negatively charged electro

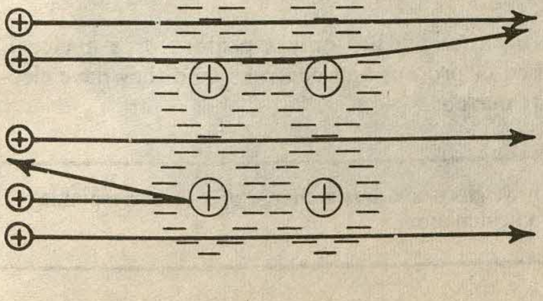


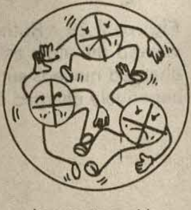
Figure 2.30 Model explaining the results of Rutherford's experiment.

equivalent to that inside the Astrodome (the atom) surrounded by some mosquitoes (electrons) who flit here and there throughout the stadium.

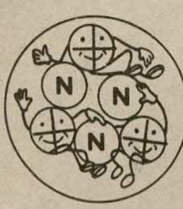
The nuclear theory lent a new interpretation to chemical reactions. The nucleus remains unchanged during a chemical reaction. It is the surrounding cloud of electrons that is altered. For example, electrons can be removed or added to the "surface" of the atom, and positive or negative ions can be formed.

Figure 2.31 Neutrons help hold larger nuclei together.

Hydrogen



Larger atom with three protons and no neutrons



Larger atom with three protons and three neutrons

2.9 The Elusive Neutron

In 1914, Rutherford suggested that the smallest positive ray particle (i.e., that which is formed when there is hydrogen gas in the Goldstein apparatus) be taken as the unit of positive charge in the nucleus. This particle, called a *proton*, has a charge equal in magnitude to that of the electron and has nearly the same mass as the hydrogen atom. Rutherford's suggestion was that protons constitute the positively charged matter in all atoms. The hydrogen atom's nucleus consisted of one proton, and the nuclei of larger atoms contained a number of protons. Except for hydrogen atoms, though, atomic nuclei were found to be heavier than would be indicated by the number of positive charges (number of protons). For example, the helium nucleus was found to have a charge of 2+ (and, therefore, it contained two protons, according to Rutherford's theory), but its mass was four times that of hydrogen. This excess weight puzzled scientists until 1932, when the English physicist James Chadwick discovered a particle with about the same mass as a proton, but with *no* electrical charge. This particle was called the *neutron*, and its existence made possible an explanation of the unexpectedly high weight of the helium nucleus. Whereas the hydrogen nucleus contained only a proton, weighing 1 atomic mass unit (amu), the helium nucleus contained not only two protons (2 amu) but also two neutrons (2 amu), giving a total weight to the nucleus of 4 amu.**

One can even offer a rationale for the presence of neutrons in the helium nucleus and in the nuclei of bigger atoms. The nucleus is very small and two protons have to get very close together within it. Perhaps the neutrons act as a sort of buffer between the protons to ease the repulsive forces experienced by the two like-charged protons. Hydrogen, with only one proton, doesn't really need a neutron—a neutron would not hurt the hydrogen nucleus, but the single proton in hydrogen doesn't really require buffering of any sort.

With the discovery of the neutron, the list of "building blocks" we will need for "constructing" atoms is complete. The properties of these particles are summarized in **table 2.4.**

All atoms, except hydrogen (which has only a proton for a nucleus), have a tiny nucleus composed of protons and neutrons, and they have electrons somewhere outside the nucleus.

*The alpha particle, which weighs 4 and has a charge of 2+, corresponds exactly to the nucleus of a helium atom.

Table 2.4
Subatomic particles

Particle	*Symbol*	*Mass (in atomic mass units)*	*Charge*	*Location in Atom*
Proton	p	1	1+	Nucleus
Neutron	n	1	0	Nucleus
Electron	e	$\frac{1}{1837}$	1−	Outside nucleus

Figure 2.32 The rain an example of a continu spectrum.

2.10 Electronic Structure: The Danish Modern Atom

First, an aside. Light, such as that emitted by the sun or an incandescent bulb, is a form of pure energy. When white light from an incandescent lamp is passed through a prism, it is separated into a continuous spectrum, or rainbow, of colors (**figures 2.32** and **2.33**). When sunlight passes through a raindrop, the same phenomenon occurs. The different colors of light represent different amounts of energy. Blue light packs more energy than does red light of the same intensity. White light is simply a combination of all the various colors of different energies.

Now back to atoms. If the light from a flame in which a certain element is being heated is passed through a prism, only narrow colored lines are obtained (**figure 2.34**). Each line corresponds to light of definite energy. The pattern of colored lines emitted by each element (called its line spec-

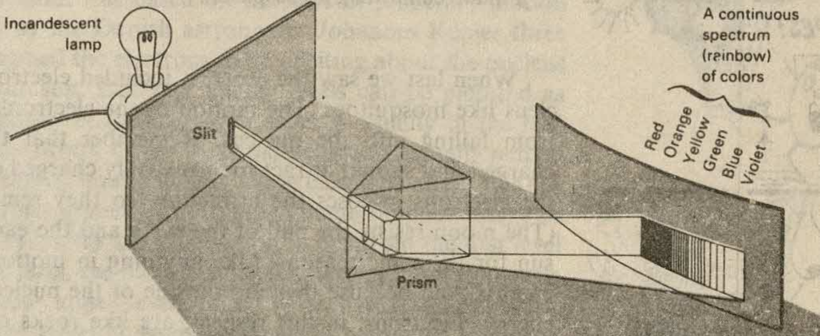


Figure 2.33 White light is sepa into a continuous spect

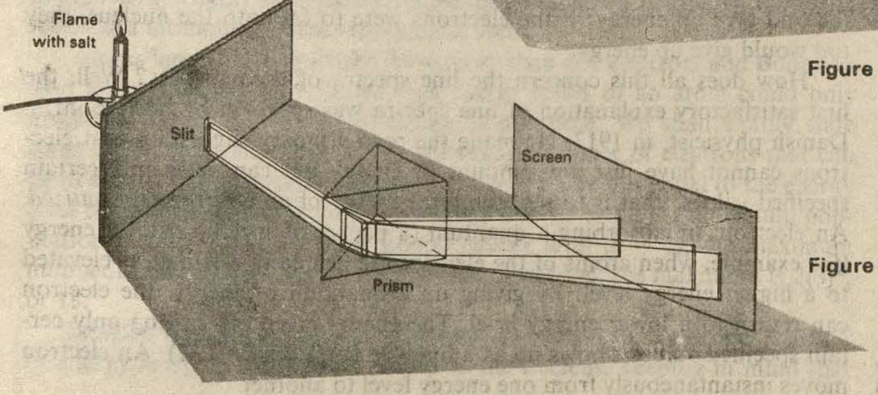
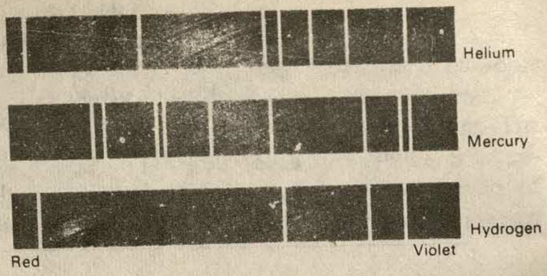


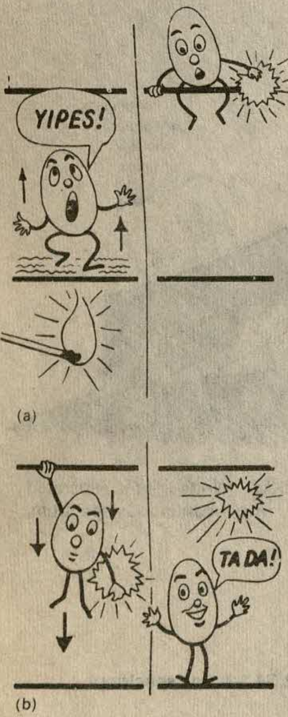
Figure 2.34 A line spectrum.

Figure 2.35 Characteristic line spectra of some elements.



trum) is characteristic of that element and can be used to identify it (**figure 2.35**). Consider, for example, the fact that the only thing reaching the earth from the stars or the planets is light. Until recently, everything we knew about these heavenly bodies had to be deduced from our examination of this light. Scientists have used line spectra to determine the chemical makeup of the stars and the atmospheres of the planets.

Figure 2.36 The processes of absorption and emission of energy by atoms are quantized. (a) When heated in a flame, an atom can absorb a quantum of energy, and the electron will jump to a higher energy level. (b) The electron will eventually jump back to the lower energy level spontaneously, releasing the quantum of light in the process.


YIPES!
(a)
TA DA!
(b)

In a crude way, the color of a flame can be used to identify an element. Sodium salts give a persistent yellow color. Potassium salts give a fleeting lavender color. Barium salts give a yellow-green color; copper salts, a bright green. There is a story, perhaps apocryphal, of a worker in a chemical plant who suspected that food left on the plate wound up in the next day's soup. He put lithium chloride on his leftovers one day. Liquid from the soup the next day burned with the telltale brilliant red flame that indicates lithium, confirming his suspicion.

When last we saw the atom, it included electrons flitting about the nucleus like mosquitoes. The motion of the electrons, by the way, kept them from falling into the nucleus. Remember that the nucleus is positively charged and should attract the negatively charged electrons. The motion of the electrons opposes the attraction, so they remain outside the nucleus. (The moon resists the pull of the earth and the earth does not fall into the sun for the same reason.) Like anything in motion, electrons have kinetic energy. And because they are outside of the nucleus, they have a potential energy. Electrons, in this respect, are like rocks on a cliff. The rocks can fall and give up energy; if the electrons were to fall into the nucleus, they too would give up energy.

How does all this concern the line spectra of the elements? Well, the first satisfactory explanation of line spectra was set forth by Niels Bohr, a Danish physicist, in 1913. He made the revolutionary suggestion that electrons cannot have just any amount of energy but can have only certain specified values; that is to say, the total energy of an electron is *quantized*. An electron, by absorbing a quantum (a packet of specific size) of energy (for example, when atoms of the element are heated in a flame), is elevated to a higher energy level. By giving up a quantum of energy, the electron can return to a lower energy level. The energy given off, having only certain specified values, shows up as a line spectrum (**figure 2.37**). An electron moves instantaneously from one energy level to another.

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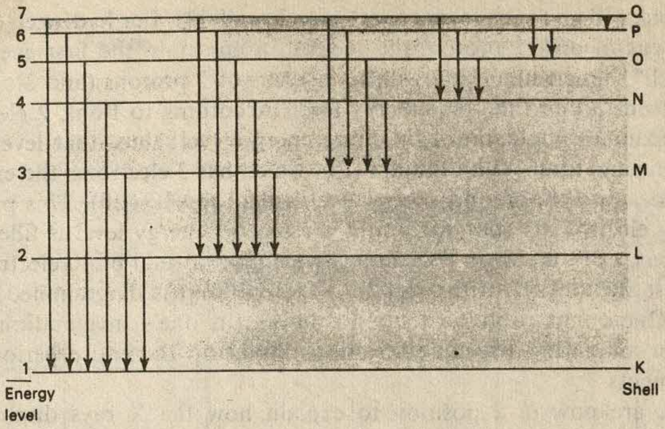

Figure 2.37 Possible electron shifts between energy levels in atoms to produce the lines found in spectra. Not all the lines are in the visible portion of the spectrum. Energy levels are sometimes called "shells" and are lettered as indicated on the right of the figure.

An analogy would be that of a person on a ladder. The person can stand on the first rung, the second rung, the third rung, and so on but is unable to stand between rungs. As the person goes from one rung to another, the potential energy (energy due to position) changes by definite amounts, or quanta. For an electron, its total energy (both potential and kinetic) is changed as it moves from one energy level to another.

Bohr's model of the atom was based on the laws of planetary motion that had been set down by the Danish astronomer Johannes Kepler three centuries before. He imagined the electrons to be orbiting about the nucleus much as planets orbit the sun. Different energy levels can be pictured as different orbits. The electron in the hydrogen atom is usually in the first energy level (the innermost orbit). Given the choice, electrons usually remain in their lowest possible energy levels; atoms whose electrons are in this situation are said to be in their *ground state*. When a flame supplies energy to an atom (hydrogen, for example) and its electron jumps from the first level to the second or a higher level, the atom is said to be *excited*. An atom with its electron in one of these upper levels or in an excited state eventually emits energy (light) as the electron jumps back down to one of the lower levels and ultimately reaches the ground state.

Atoms larger than hydrogen have more than one electron, and Bohr was also able to deduce that the various energy levels of an atom could only handle a certain number of electrons at one time. We shall simply state Bohr's findings in this regard. The maximum number of electrons that can be in a given level is given by the formula $2n^2$, where n is equal to the energy level being considered. For the first energy level ($n = 1$), the maximum population is $2(1)^2$, or 2. For the second energy level ($n = 2$), the maximum number of electrons is $2(2)^2$, or 8. For the third level, the maximum is $2(3)^2$, or 18.

Imagine building up atoms by adding 1 electron to the proper "shell," or energy level, as protons are added to the nucleus, keeping in mind that

Figure 2.38 Quantum
sorption. Change of posit
requires a quantum of en
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electrons will go to the lowest energy level available. For hydrogen (H), with a nucleus of only 1 proton, the 1 electron goes into the first energy level (K shell*). For helium (He), with a nucleus of 2 protons (and 2 neutrons), 2 electrons go into the first energy level. According to Bohr, 2 electrons is the maximum population of the first energy level; thus, that level is filled in the helium atom. With lithium (Li), which has 3 electrons, the extra electron goes into the second energy level (called the L shell). This process of adding electrons is continued until the second energy level is filled with 8 electrons, as in the neon (Ne) atom (which has a total of 10 electrons, 2 in the first shell and 8 in the second). This buildup is diagrammed in **figure 2.41.** One could continue to build atoms (in one's imagination) in this manner and, with a few modifications, build up the entire periodic chart of elements.

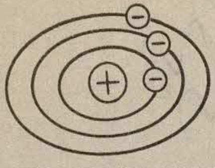
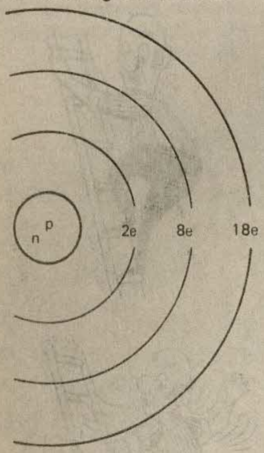


Figure 2.39 Bohr visualized the atom as planetary electrons circling a nuclear sun.

We are now in a position to explain how the X rays discovered by Roentgen originated. We have already indicated that the cathode rays (streams of electrons knocked from the atoms in the cathode) can knock other electrons from the atoms of gas in the gas discharge tube. High-energy cathode rays strike electrons in the inner energy levels of atoms, dislodging them from the atom (particularly the atoms of the anode). Outer electrons in these atoms then cascade down into the vacant inner levels, giving up energy in the form of X rays as they do so. The pattern of X rays emitted by atoms of a particular element is as characteristic of the element as its line spectrum.

Figure 2.40 A shorthand drawing of a Bohr atom.



2.11 Energy Levels and the Periodic Table

The properties of atoms depend mainly on the number of electrons in the outermost energy level. Sodium (Na) is the element immediately after neon; therefore, it has one more electron than neon and must place this electron into the third energy level. Sodium, with one electron in its outermost level (the third, or M, shell) is similar in properties to lithium, which also has only one electron in its outermost level (the second, or L, shell). Helium and neon, having filled outer shells, are similar to each other in that both are inert, that is, in that they tend not to undergo reactions. Apparently, not only do similar chemical properties occur in atoms of similar electronic

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*One of the most exasperating things about the subject of chemistry for the nonchemist (and, for that matter, the chemist) is the complication of terminology. For example, why, having established a perfectly reasonable naming system for energy levels (called *1, 2, 3,* and so on, from lowest to highest), do we now mention that these same levels are also referred to as *K, L, M,* and so on? The trouble here is that the concepts were developed over a period of time, and people who were working on different aspects of the same problem invented different terminologies. When the problem was solved, it was realized that *K, L,* and *M* referred to precisely the same thing as *1, 2,* and *3.* By that time, however, some people were so used to using *K, L,* and *M* that it was difficult to convince them to use *1, 2,* and *3.* The same attachment to familiar terms is what makes some people call meteors "shooting stars."

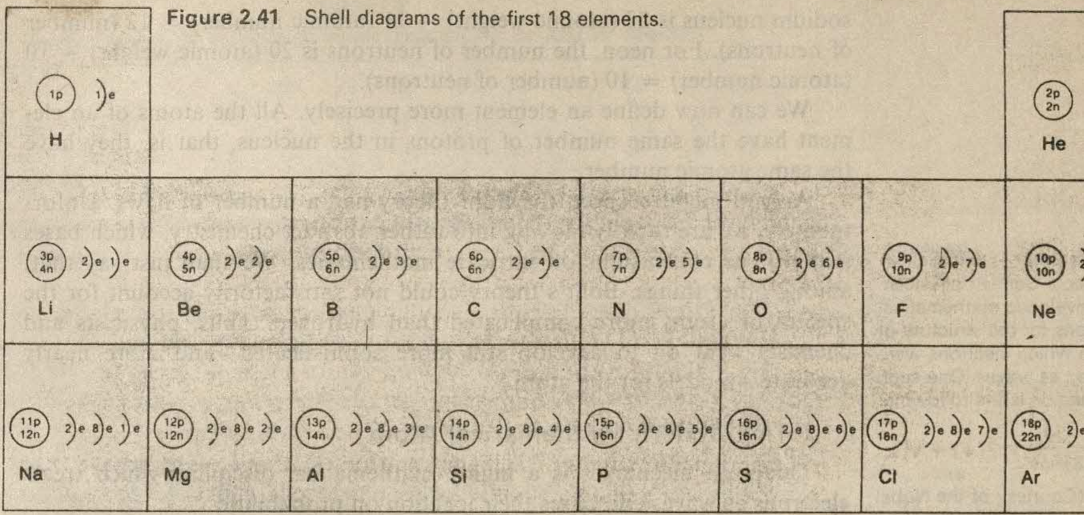
Figure 2.41 Shell diagrams of the first 18 elements.

configuration (or arrangement), but certain configurations appear to be more stable (more unreactive) than others. This is a point we shall explore in detail in chapter 4.

The modern periodic chart differs from that of Mendeléev in that the elements are arranged according to *atomic number*. This number gives the number of protons, which for a neutral atom is the same as the number of electrons. Mendeléev had arranged the elements by chemical properties, which he found to parallel atomic weights roughly. However, it is the number of electrons that determines chemical properties and that should (and now does) determine the order of the periodic table. Increase in atomic weight roughly parallels increase in atomic number, and in only a few cases (such as those noted by Mendeléev) do the weights fall out of order. The reason atomic weights do not increase in precisely the same order as atomic number is that weights of atoms are primarily determined by the number of protons *and* neutrons. And neutrons are not added to atoms in quite the same orderly fashion that protons and electrons are.

The number of neutrons* in an atom can be calculated by subtraction of the atomic number from the atomic weight and rounding of the latter to the nearest whole number. For example, the number of neutrons in the

*Atoms of most elements have varying numbers of neutrons in the nucleus. For example, all carbon atoms have six protons in their nucleus (or else they would not be carbon atoms), but some have six neutrons, some have seven, and others have eight. This results in the existence of isotopes—atoms of the same element with different weights. The procedure described here for determining the number of neutrons in an element gives a value corresponding to the most common isotopes of elements of the first three periods of the periodic table. Isotopes are discussed in more detail in the next chapter.

sodium nucleus is 23 (atomic weight) − 11 (atomic number) = 12 (number of neutrons). For neon, the number of neutrons is 20 (atomic weight) − 10 (atomic number) = 10 (number of neutrons).

We can now define an element more precisely. All the atoms of an element have the same number of protons in the nucleus, that is, they have the same atomic number.

As you might suspect, the Bohr theory had a number of flaws. Unfortunately, we are rapidly moving into rather abstract chemistry, which bases many of its conclusions on intricate mathematics. We shall just say that, among other things, Bohr's theory could not satisfactorily account for the spectra of atoms more complicated than hydrogen. Thus, physicists and chemists went on to develop still more sophisticated—and more nearly accurate—models for the atom.

Figure 2.42 Erwin Schrödinger, a German physicist, developed mathematical equations for the structure of atoms in which electrons were treated as waves. One such equation is the following.

$$E(\psi) = \frac{-h^2}{8\pi^2 m}\nabla^2(\psi) + V(\psi)$$

(Courtesy of the Nobel Institute, Stockholm.)

2.12 The Modern Mathematical Atom

Quantum mechanics is a highly mathematical discipline which treats electrons as waves and bases their location on probabilities.

It was the young French physicist Louis de Broglie who first suggested (in 1925) that the electron had wavelike properties. In other words, de Broglie said that a beam of electrons should behave like a beam of light. Since Thomson had "proved" (in 1897) that electrons were particles and not light, this suggestion that they be treated as waves was hard to accept. Nevertheless, de Broglie's theory was experimentally verified within a few years. (J. J. Thomson's son was one of those who provided evidence that verified de Broglie's theory.) Electron microscopes, which make use of the wave nature of electrons, are now very important pieces of equipment in many scientific laboratories.

A model of the atom, based on this wave nature of the electron, was developed in the late 1920s, principally by the German physicist Erwin Schrödinger (**figure 2.42**). Elaborate equations which describe the properties that the electron waves in atoms have are fundamental to the modern picture of the atom. Solutions to these equations are called *wave functions*. These wave functions can be manipulated to provide a measure of the probability that an electron is located in a given volume of space. The definite planetary orbits of the Bohr atom are abandoned* in favor of three-dimensional charge clouds—volumes of space in which the electrons move. These clouds are referred to as *orbitals* to distinguish them from Bohr's orbits.

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*It is interesting to note, however, that the figure given by Bohr for the radius of the first orbit, 52.9 picometres (pm), is the same as the "most probable" distance from the nucleus of an electron in the first energy level—as revealed by wave mechanical calculations. Here is a point worth commenting on. A new theory replaces an old one when the new theory explains something the old one can't. However, the new theory must also answer all those questions the old theory was able to handle, and the new answers must be at least as good as the old.

Table 2.5

Composition of the commonest atoms (isotopes) of the first 10 elements

	H	*He*	*Li*	*Be*	*B*	*C*	*N*	*O*	*F*	*Ne*
Number of protons	1	2	3	4	5	6	7	8	9	10
Number of electrons	1	2	3	4	5	6	7	8	9	10
Number of neutrons*	0	2	4	5	6	6	7	8	10	10

*Note that, although the number of neutrons generally increases, it does not follow the same regular increase as the number of protons and electrons.

The calculations involved in the solution of wave equations are complicated and time-consuming. We don't need to be able to do these elaborate calculations, however, in order to use some of the results of quantum mechanics. For example, a plot of the electron probability distribution of electrons in the lowest energy level always has a spherical symmetry. If that sentence is meaningless to you, try this. Suppose you had a camera which could photograph electrons (there is no such thing, but we are just supposing) and you left the shutter open while the electron zipped about the nucleus. When you developed the picture you would have a record of where the electron had been. Doing the same thing with an electric fan which was turned on would give you a picture in which the blades of the fan looked like a solid disk of material. The blades move so rapidly that their photographic image is blurred. Back to the electrons. This imagined picture of electrons in the first energy level would look like a fuzzy ball (that's what *spherical symmetry* means). The quantum mechanical orbital corresponds to this fuzzy ball (**figure 2.43**). Orbitals such as this are designated 1*s*, and, like Bohr's lowest energy level, the 1*s* orbital can contain only two electrons.

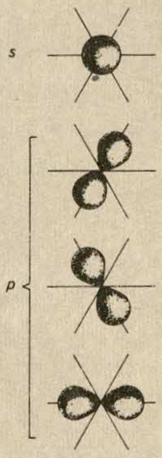
An *s* orbital

A *p* orbital

Figure 2.43 Charge cloud representations of atomic orbitals.

Quantum mechanical calculations split the second lowest energy level (which, like Bohr's, can hold eight electrons) into four different orbitals. The first two electrons in the second energy level also have spherical symmetry. The orbital for these two electrons is designated 2*s* (2 because it is in the second energy level, *s* because it is spherical, like the 1*s* orbital). The next six electrons of the second energy level go into three orbitals that are dumbbell shaped (**figure 2.44**) and differ from one another only in the direction in which they point. These are designated the 2*p* orbitals. Again, the 2 indicates that these orbitals are in the second energy level and the *p* means that they have the dumbbell shape. To distinguish the different *p* orbitals, they are sometimes referred to as the $2p_x$, $2p_y$, and $2p_z$ orbitals.

Figure 2.44 Outline representations of atomic orbitals. The three *p* orbitals differ only in their orientation in space.



An orbital can be occupied by 1 electron or by 2 paired electrons, but no more. Thus, the 2 electrons of the lowest energy shell can be accommodated by the 1*s* orbital. The second shell requires four different orbitals to accommodate its 8 electrons. The third shell (with 18 electrons) requires nine orbitals: a 3*s* orbital, three 3*p* orbitals, and a new set of orbitals, the 3*d*, of which there are five. We shall not bother to draw all of these orbitals. The point is that each energy level has more orbitals than the one below it, in order to accommodate the larger number of electrons in the higher energy levels.

Table 2.6
Models of the atom

Dalton's model	Billiard ball model—Atom a hard, indestructible particle with a particular weight
Thomson's model	Raisin pudding model—Atom subdivided into positive and negative parts
Rutherford's model	Nuclear atom model—Atom composed of positive parts (protons) in tiny nucleus and negative parts (electrons) situated throughout its mostly empty volume
Chadwick's modification	Atom modified to include neutrons in its nucleus
Bohr's model	Planetary atom model—Atom with electrons assigned to very specific orbits (energy levels)
Schrödinger's model	Quantum mechanical atom—Atom with orbitals in three dimensions

Strictly speaking, these various orbitals would have to be infinite in size to account for an electron with 100% certainty. Quantum mechanics states that there is at least a tiny probability that any electron can be anywhere in the universe. For convenience in representing orbitals, however, an outline drawing is used to indicate a 95% probability that the electron is located within the volume so outlined (see figure 2.44).

The mathematical picture of the atom has grown quite abstract in recent years. The atomic physicist sometimes seems to say that only the mathematics are real, not the atom.

For our purposes, we will use whatever model is most helpful for understanding a particular concept. In trying to evaluate the behavior of gases, chemists often use Dalton's hard, indivisible (billiard ball) model. In discussing how atoms combine to form molecules, we will use the Bohr model for the most part. To explain the shape of molecules (very important in explaining the action of drugs, for instance) we will use an extension of the Bohr theory called the valence shell electron pair repulsion (VSEPR) theory for the most part. Occasionally we will employ the orbital atom theory. Don't let this inconsistent use disturb you. Remember that a model or a theory is used to explain phenomena. When a better model or theory is invented, the old is sometimes discarded or pushed into a secondary role, but occasionally it can be used to clarify some point which a newer, more complicated model only obscures.

Problems

1. Why did the majority of the Greek philosophers believe in the continuity of matter?
2. Why couldn't Democritus prove his atomistic theory?
3. What is a scientific "law"? How does a scientific law differ from a governmental law?
4. What is a theory?
5. How does the Greek view of an element differ from the modern view?
6. Discuss evidence indicating the electrical nature of matter.

7. Explain, in terms of Dalton's atomic theory, the law of conservation of mass, the law of definite proportions, and the law of multiple proportions. Illustrate each law by an example.
8. When 18 g of water are decomposed by electrolysis, 16 g of oxygen and 2 g of hydrogen are formed. According to the law of definite proportions, how much hydrogen would be formed by the electrolysis of 180 g of water? Hydrogen, from the decomposition of water, has been promoted as the fuel of the future. How many tonnes* of water would have to be electrolyzed for 2 tonnes (t) of hydrogen to be produced? How much would have to be electrolyzed for 1 t of hydrogen to be produced?
9. Carbon can burn in air to form either carbon monoxide or carbon dioxide, depending upon the amount of oxygen present during combustion. Using the weight ratios given on page 20, calculate how much carbon would have to be burned for the following to be produced.
    a. 70 g of carbon monoxide
    b. 1100 g of carbon dioxide
10. The gas silane can be decomposed to yield silicon and hydrogen in a ratio of 7 parts of silicon by weight to 1 part of hydrogen by weight. If the relative weight of silicon atoms is 28 when the weight of hydrogen is taken to be 1, how many hydrogen atoms are there combined with each silicon atom?
11. Jan Baptista van Helmont, a Flemish alchemist (1579–1644), performed an experiment in which he planted a young willow tree in a weighed bucket of soil. After 5 years, he found that the tree had gained 75 kg yet the soil had lost only 57 g (0.057 kg). Van Helmont had added only water to the system. He concluded that the substance of the tree had come from water. Criticize van Helmont's conclusion.
12. What evidence is there that electrons are particles?
13. What caused Thomson's model of the atom to be discarded?
14. Discuss the role of serendipity in scientific discovery.
15. Without referring to **table 2.5**, indicate how many electrons, how many protons, and how many neutrons there are in a neutral atom of each of these elements. (You may use the periodic chart.)
    a. calcium (Ca)
    b. fluorine (F)
    c. beryllium (Be)
    d. sodium (Na)
    e. argon (Ar)
    f. nitrogen (N)
16. Consulting only the periodic chart, draw electron shell diagrams for these elements.
    a. helium (He)
    b. magnesium (Mg)
    c. carbon (C)
    d. sulfur (S)
    e. oxygen (O)
    f. silicon (Si)
17. What is the maximum number of electrons in the fourth energy level ($n = 4$)?
18. What is the difference between a Bohr "orbit" and the "orbital" of wave mechanics?
19. Referring only to a periodic table, indicate what similarity in electronic structure is shared by fluorine (F) and chlorine (Cl) and by carbon (C) and silicon (Si). What is the difference in their electronic structures? What is the difference in the electronic configurations of oxygen (O) and fluorine (F)?
20. Elements are defined on a theoretical basis as being composed of atoms all of which have the same atomic number. On the basis of this theory, would you think it possible for someone to discover a new element that would fit between magnesium (whose atomic number is 12) and aluminum (whose atomic number is 13)?

*The SI unit tonne is 1000 kg. It is also referred to as the "metric ton." The tonne is 2204 lb, slightly less than the "long ton" (2240 lb).

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chapter 3

Nuclear Processes

In chapter 2 we took a brief look at the atomic nucleus and then turned our attention outward to electrons. For a major portion of this book, we will take special note of the outermost electrons. It is the interaction of these particles that holds atoms together to make up the materials of the world as we know them. For the moment, however, let us turn our gaze inward to that tiny, tiny speck of matter called the nucleus.

Atomic nuclei are 10 000 times smaller than whole atoms, yet it is the nucleus that holds the power which has become the symbol of our age. Nuclear power, unleashed in wrath, can destroy cities—perhaps civilizations. Nuclear power controlled can provide part of the energy necessary for the maintenance of cities and civilizations, although there are potential problems in its use.

Nuclear bombs kill. Nuclear medicine saves lives. Diseases once regarded as incurable can be effectively diagnosed and treated with radioactive isotopes. Applications of nuclear chemistry in biology, industry, and agriculture have significantly improved the human condition. The use of radioisotopes in biological and agricultural research has led to increased crop production, providing more food for a hungry world.

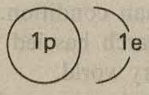
The nuclear age is a paradox. It is both frightening and reassuring. Knowledge of nuclear science has given us a greater power than ever before in human history. To get your share of the power, you must get your share of the knowledge. Your decisions as an informed citizen may determine whether future generations recall the nuclear age with fond regard or deep regret. Those decisions may even determine whether future generations exist.

3.1 A Partial Parts List for the Atomic Nucleus

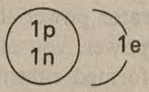
We saw in chapter 2 that atomic nuclei are made up of protons and neutrons. Although the nuclear physicists have extended this parts list to more than a hundred particles, most of these have a transitory existence and are of little interest to a chemist. We shall take the oversimplified, but useful, view that atomic nuclei are made up of protons and neutrons—and some sort of force that holds them together.

A proton and neutron have virtually the same mass—1.007276 amu and 1.008665 amu, respectively. That's equivalent to saying that two different people weigh 100.7 lb and 100.9 lb. The difference is so small it can be ignored. Thus, for many purposes, we assume the masses of the proton and the neutron to be the same—1 amu each. The proton has a charge equal in magnitude but opposite in sign to that of an electron. This charge on a proton is written as 1+. The electron has a charge of 1− and a mass of 0.000549 amu. The electrons in an atom contribute so little of its total mass that they are usually disregarded and are treated as if their mass were 0. The subatomic particles of greatest interest to us are summarized in **table 3.1.**

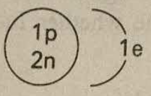
The number of protons in the nucleus of an atom of any element is the atomic number of that element. This number determines the kind of atom, that is, the element. For example, an atom with 26 protons (one whose atomic number is 26) is an atom of iron (Fe). An atom with 92 protons is an atom of uranium (U). (You are not expected to memorize the atomic number of every element. But you should be able to find this information in a periodic table.) The number of neutrons in the nucleus of atoms of a given element may vary. Most hydrogen (H) atoms have a nucleus consisting of a single proton and no neutrons. About 1 hydrogen atom in 5000, however, does have a neutron as well as a proton in the nucleus. Both kinds are hydrogen atoms (any atom with atomic number 1, that is, with one proton, is a hydrogen atom). Atoms that have this sort of relationship—the same number of protons but differing numbers of neutrons—are called *isotopes.* There is a third, very rare isotope of hydrogen, called tritium, which has two neutrons and one proton in the nucleus. Most, but not all, elements exist in nature in isotopic forms. An interesting and easy-to-remember example is the element tin (Sn), which exists in 10 isotopic forms. (Tin . . . ten. Get it?)



Ordinary hydrogen (sometimes referred to as protium to distinguish it from other isotopes)



Deuterium (heavy hydrogen)



Tritium (very heavy hydrogen?)

Isotopes are of little importance in ordinary chemical reactions. That simply means that the existence of different isotopes of any element has essentially no effect on the course of a chemical reaction and little effect

Table 3.1
Subatomic particles

Particle	*Symbol*	*Approximate Mass*	*Charge*
Proton	p	1	1+
Neutron	n	1	0
Electron	e	0	1−

on the rate of a chemical reaction. Both light (ordinary) hydrogen atoms and heavy hydrogen (deuterium) atoms react with oxygen to form water. Since deuterium atoms are about twice as heavy as ordinary hydrogen, compounds formed from the two different isotopes have different physical properties, but such differences are usually slight. *Chemical reactions* involve the outer electrons of an atom. Differences in the number of neutrons buried deep in the heart of the atom would not be expected to have a major effect. However, in *nuclear reactions*, reactions which do involve the heart of the atom, isotopes are of utmost importance, as we shall see later in this chapter.

3.2 Nuclear Arithmetic

Before we talk about nuclear reactions, it will be necessary to discuss a special symbolism used in writing such reactions. To represent different isotopes, symbols with subscripted and superscripted numbers are used. In the generalized symbol

$${}^{A}_{Z}\mathrm{X}$$

the Z represents the *atomic number*, that is, the number of protons. The A represents the *mass number*, the number of protons plus the number of neutrons. From the symbol

$${}^{35}_{17}\mathrm{Cl}$$

we know that the number of protons is 17. The number of neutrons is 18 (35 − 17).

The Z number is not really necessary, since the elemental symbol establishes the number of protons in the nucleus being considered. However, it is convenient to have this information at one's fingertips while writing nuclear reactions.

Example 3.1 How many neutrons are there in the ${}^{235}_{92}\mathrm{U}$ nucleus?

235 (mass number) − 92 (atomic number) = 143 (number of neutrons)

Example 3.2 Which of the following are isotopes of the same element? We are using the letter X as the symbol for all so that the symbol will not identify the elements.

$${}^{16}_{8}\mathrm{X} \quad {}^{16}_{7}\mathrm{X} \quad {}^{14}_{7}\mathrm{X} \quad {}^{14}_{6}\mathrm{X} \quad {}^{12}_{6}\mathrm{X}$$

$^{16}_{7}X$ and $^{14}_{7}X$ are isotopes of the element nitrogen (N). $^{14}_{6}X$ and $^{12}_{6}X$ are isotopes of the element carbon (C).

Which of the original five isotopes have identical mass numbers?

$^{16}_{8}X$ and $^{16}_{7}X$ have the same mass number. The first is an isotope of oxygen and the second is an isotope of nitrogen. $^{14}_{7}X$ and $^{14}_{6}X$ have the same mass number. The first is an isotope of nitrogen and the second is an isotope of carbon.

Which of the original five isotopes have the same number of neutrons?

$^{16}_{8}X$ (16 − 8 = 8 neutrons) and $^{14}_{6}X$ (14 − 6 = 8 neutrons) have the same number of neutrons.

3.3 Natural Radioactivity

Some nuclei are unstable as they occur in nature. Radium atoms with a mass number of 226, for example, break down spontaneously, giving off *alpha* particles. Since alpha particles are identical to helium nuclei, this process may be summarized by the equation

$$^{226}_{88}\mathrm{Ra} \longrightarrow {}^{4}_{2}\mathrm{He} + {}^{222}_{86}\mathrm{Rn}$$

or

$$^{226}_{88}\mathrm{Ra} \longrightarrow \alpha + {}^{222}_{86}\mathrm{Rn}$$

The new element, with two fewer protons, is identified by its atomic number (86) as radon (Rn). Note that the mass number of the reactant must equal the sum of the mass numbers of the products. The same is true for the atomic numbers. The use of the symbol $^{4}_{2}\mathrm{He}$ for the alpha particle is preferred to the symbol α because the former allows one to check the balance of mass and atomic numbers more readily.

Thorium nuclei are also unstable. The isotope with a mass number of 234 decomposes by what is termed *beta decay*. Since a beta particle is identical with an electron, this process may be written

$$^{234}_{90}\mathrm{Th} \longrightarrow {}^{\;0}_{1-}\mathrm{e} + {}^{234}_{91}\mathrm{Pa}$$

or

$$^{234}_{90}\mathrm{Th} \longrightarrow \beta^- + {}^{234}_{91}\mathrm{Pa}$$

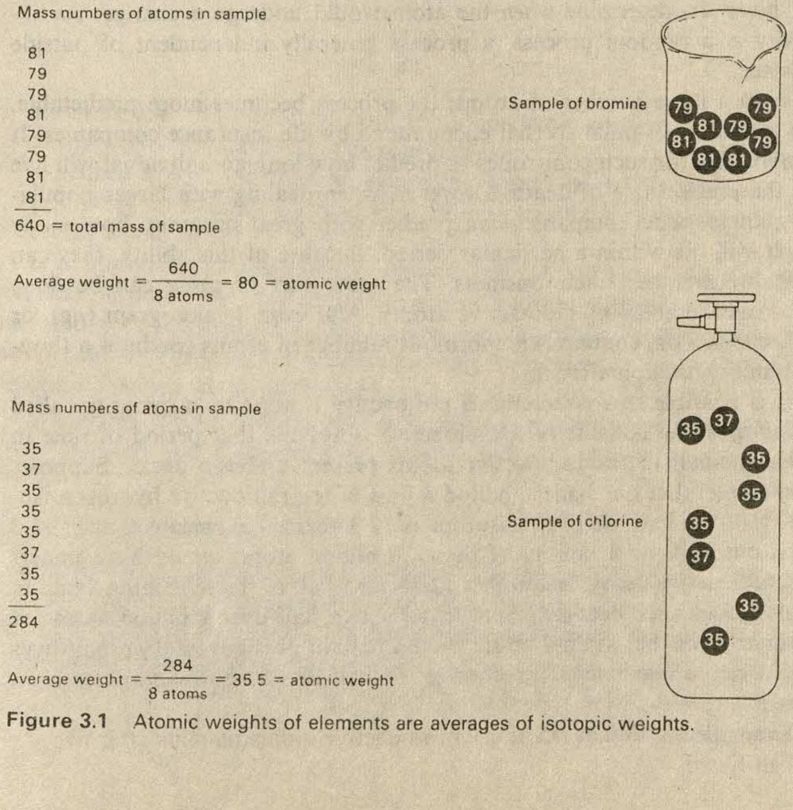
The new element, with one more proton, is identified by its atomic number as protactinium (Pa). How can the original nucleus, which contains only protons and neutrons, emit an electron? One can envision one of the neutrons in the original nucleus changing into a proton and an electron.

$$^{1}_{0}\mathrm{n} \longrightarrow {}^{1}_{1}\mathrm{p} + {}^{\;0}_{1-}\mathrm{e}$$

The new proton is retained by the nucleus (therefore the atomic number of the product increases by 1), and the almost massless electron or beta particle is kicked out (the product nucleus has the same mass as the original).

The *mass number* gives the mass of the particular isotope. The *atomic mass*, or *atomic weight*, of an element, as listed in the periodic table, is related to the mass number in the following way. The atomic mass, or weight, is the average weight of the atoms in a representative sample of an element. Each individual atom of such a sample has a particular mass number. For example, in a sample of the element bromine, about half the atoms have a mass number of 79 and half have a mass number of 81. The atomic weight of bromine is about 80, the average of 79 and 81. (The atomic weight of bromine is actually 79.9, indicating that there is slightly more of the bromine-79 isotope than of the bromine-81.) Another example: about three-quarters of the atoms of the element chlorine have a mass number of 35, and about one-quarter have a mass number of 37. The atomic weight of chlorine is 35.5; the average mass in this case is much closer to that of the chlorine-35 isotope because of the preponderance of this isotope in the sample (**figure 3.1**).

The third type of radioactivity is called *gamma decay*. No particle is emitted; remember, gamma rays are related to light. Gamma emission involves no change in atomic number or mass. The process is analogous to the emission of light from an atom. In that case, light is emitted when an electron in an excited state drops to a lower energy level. In gamma emission a nucleus in an excited state drops to a lower energy state. This type of decay is particularly useful when radioisotopes (radioactive isotopes) are used for



Mass numbers of atoms in sample

81
79
79
81
79
79
81
81

640 = total mass of sample

$$\text{Average weight} = \frac{640}{8 \text{ atoms}} = 80 = \text{atomic weight}$$

Mass numbers of atoms in sample

35
37
35
35
35
37
35
35

284

$$\text{Average weight} = \frac{284}{8 \text{ atoms}} = 35.5 = \text{atomic weight}$$

Figure 3.1 Atomic weights of elements are averages of isotopic weights.

Table 3.2
Radioactive decay and nuclear change

Type of Radiation	Symbol	Mass Number	Charge	Change in Mass Number	Change in Atomic Number
Alpha	α	4	2+	Decreases by 4	Decreases by 2
Beta	β	0	1−	No change	Increases by 1
Gamma	γ	0	0	No change	No change

diagnostic purposes in medicine. We will discuss such uses later in this chapter. Gamma emission frequently accompanies the emission of alpha or beta particles.

The major types of radioactive decay and the ensuing nuclear changes are summarized in **table 3.2**.

3.4 Half-Life

Thus far we have discussed radioactivity as applied to single atoms. In the laboratory one generally deals with great numbers of atoms—numbers far larger than the number of people on earth. If we could see the nucleus of an individual atom, we could note its composition and tell *whether* or not it would undergo radioactive decay. Previous observations have indicated that certain combinations of protons and neutrons are unstable. We could not, however, determine *when* the atom would undergo a change. Radioactivity is a random process, a process generally independent of outside influence.

With a large number of atoms, the process becomes more predictable. The situation is similar to that encountered by life insurance companies. It is impossible for such companies to predict how long an individual will live and the precise date of death. However, when dealing with larger populations, these same companies can predict with great accuracy how many people will die within a particular period. Because of this ability, they can profitably maintain their business. The same sort of thing can be done with large numbers of radioactive atoms. And even 1 microgram (μg), or 0.000 000 035 oz, contains an enormous number of atoms (perhaps a thousand million million atoms).

It is possible to characterize a radioactive isotope by a quantity called its *half-life*. The half-life of a radioactive isotope is that period of time in which one-half of the radioactive atoms present undergo decay. Suppose, for example, that one had 16 billion atoms of the radioactive hydrogen isotope, $^3_1$H. The half-life of this isotope is 12.3 years. This means that in 12.3 years, one-half, or 8 billion, of these 16 billion atoms would have undergone radioactive decay. In another 12.3 years, half of the remaining 8 billion atoms would have decayed. That is, after two half-lives 4 billion atoms or one-quarter of the original atoms would remain unchanged. Two half-lives do not make a whole! This concept of half-life is shown graphically in **figure 3.2.**

Example 3.3 What fraction of radioactive atoms remains after five half-lives?

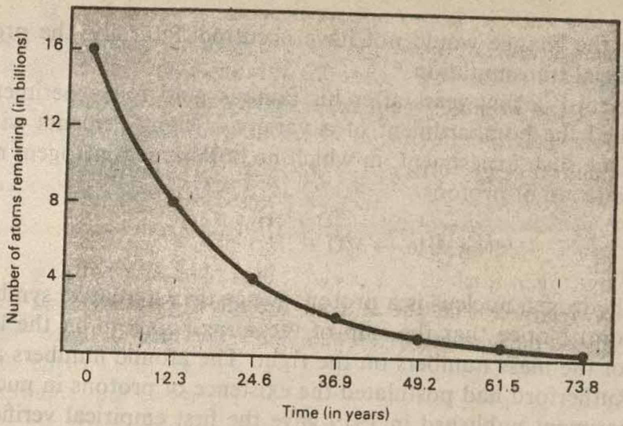


Figure 3.2 The radioactive decay of ^3_1H.

After one half-life, $\frac{1}{2}$ of the original atoms remain. After two half-lives, $\frac{1}{2} \times \frac{1}{2}$ ($\frac{1}{2}$ of $\frac{1}{2}$) $= \frac{1}{4}$ of the original atoms remain. After three half-lives, $\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = 1/(2^3) = \frac{1}{8}$ of the original atoms remain. After four half-lives, $\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = 1/(2^4) = \frac{1}{16}$ of the original atoms remain. After five half-lives, $\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = 1/(2^5) = \frac{1}{32}$ of the original atoms remain. To determine what fraction of the original sample remains after a certain number (n) of half-lives, calculate the following value.

$$\frac{1}{2^n}$$

Example 3.4 If you started with 16 million radioactive atoms, how many would you have left after four half-lives?

Since $n = 4$, the fraction remaining would be $1/(2^4)$, which is $\frac{1}{16}$, and $\frac{1}{16} \times 16$ million atoms = 1 million. A million of the original atoms would be left.

It is impossible to say exactly when *all* the ^3_1H will have decayed. For practical purposes one may assume that nearly all the radioactivity is gone after about 10 half-lives. For the tritium sample considered here, 10 half-lives would be 123 years, at which time only a fraction of a percentage of the original atoms would still be present.

The half-life of an isotope may be very long, as with $^{238}_{92}U$ (whose half-life is 4.5 billion years), or very short, as with ^9_5B (whose half-life is 8×10^{-19} seconds).

3.5 Artificial Transmutation

The forms of radioactivity encountered thus far occur in nature. Other nuclear reactions may be brought about by bombardment of stable nuclei with alpha particles, neutrons, or other subatomic particles. These particles, given sufficient energy, penetrate the formerly stable nucleus and bring about some form of radioactive emission. Like natural radioactivity, this sort of nuclear change brings about a transmutation: one element is changed into another. Because the change would not have occurred naturally, the process is called artificial transmutation.

Figure 3.3 Frédéric and Irène Joliot-Curie discovered artificially induced radioactivity in 1934. (Reprinted with permission from Weeks, Mary E., *Discovery of the Elements*, Easton, Pa.: Chemical Education Publishing, 1968. Copyright © 1968 by the Chemical Education Publishing Company.)

Ernest Rutherford, a few years after his famous gold foil experiment (chapter 2), studied the bombardment of a variety of light elements with alpha particles. One such experiment, in which he bombarded nitrogen, resulted in the production of protons.

$$^{14}_{7}N + ^{4}_{2}He \longrightarrow ^{17}_{8}O + ^{1}_{1}H$$

(Recall that the hydrogen nucleus is a proton; hence the alternative symbol $^{1}_{1}H$ for the proton.) Notice that the sum of the mass numbers on the left equals the sum of the mass numbers on the right. The atomic numbers are also balanced. Rutherford had postulated the existence of protons in nuclei in 1914. An experiment published in 1919 gave the first empirical verification of the existence of these fundamental particles. Eugen Goldstein had earlier produced protons in his discharge tube experiments (chapter 2). He obtained these particles from hydrogen gas in the tube by knocking an electron away from the hydrogen atom. The significance of Rutherford's experiment lay in the fact that he obtained protons from the nucleus of an atom other than hydrogen, thus establishing their nature as fundamental particles. By *fundamental particles* we mean basic units from which more complicated structures (such as the nitrogen nucleus) can be fashioned. Rutherford's experiment was the first induced nuclear reaction.

A great many transmutations were carried out during the 1920s. And in the 1930s one such reaction led to the discovery of another fundamental particle. James Chadwick, in 1932, bombarded beryllium with alpha particles.

$$^{9}_{4}Be + ^{4}_{2}He \longrightarrow ^{12}_{6}C + ^{1}_{0}n$$

Among the products was the neutron.

3.6 Induced Radioactivity

The first artificial nuclear reactions produced isotopes already known to occur in nature. This was perhaps fortuitous, for it was inevitable that an unstable nucleus would be produced sooner or later. Irène Curie (daughter of the 1903 Nobel Prize winners) and her husband, Frédéric Joliot, were studying the bombardment of aluminum with alpha particles. Neutrons were produced, leaving behind an isotope of phosphorus.

$$^{27}_{13}Al + ^{4}_{2}He \longrightarrow ^{30}_{15}P + ^{1}_{0}n$$

Much to their surprise, the target continued to emit particles after the bombardment was halted. The isotope of phosphorus was radioactive, emitting particles equal in mass to the electron but opposite in charge. These particles are called *positrons*. The reaction they were observing is written

$$^{30}_{15}P \longrightarrow {}^{0}_{1+}e + ^{30}_{14}Si$$

Once again the question arises: Where does this particle come from if the nucleus contains only protons and neutrons? Previously we accounted for a beta particle (an electron) popping out of a nucleus by saying a neutron changed into a proton and an electron. Perhaps a similar happening can account for the appearance of a positron. Imagine a proton changing to a neutron and a positron (a proton is the same as a hydrogen nucleus).

$${}^{1}_{1}\mathrm{H} \longrightarrow {}^{\ 0}_{1+}\mathrm{e} + {}^{1}_{0}\mathrm{n}$$

Everything balances rather nicely in this equation. When the positron is emitted, the original radioactive nucleus suddenly has one less proton and one more neutron than before. Therefore, the weight of the product nucleus is the same, but its atomic number is one less than that of the original nucleus.

This work gave the Joliot-Curies a Nobel Prize of their own in 1935. (The Joliot-Curies adopted the combined surname to perpetuate the Curie name. Marie and Pierre Curie had two daughters, but no son.)

Figure 3.4 The linear accelerator at Stanford University is 3.2 km (2.0 mi) long. (Reprinted from Pollard, William G., *The Mystery of Matter*, Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1970.)

3.7 From Out of the Blue: Cosmic Rays

Cosmic rays were discovered in 1913 by Victor Franz Hess, an Austrian physicist who made his experimental measurements as he ascended into the atmosphere in a balloon. Primary cosmic rays consist of charged particles arriving at the earth from outer space (wherever that is). Some of these particles originate at the sun, but most are believed to come from the far reaches of the Milky Way galaxy and beyond. The particles are primarily protons, with some alpha particles (helium nuclei) and some nuclei of still higher elements. They are highly energetic, some moving at nearly the speed of light. At one time, cosmic rays were used by physicists who wished to study various kinds of high-energy particles. Now giant accelerators are used to produce beams of high-energy particles for experimental studies. These instruments cost millions and even billions of dollars. In essence they are racetracks down which particles are accelerated and thus given high kinetic energy. This expenditure of money and scientific talent, however, still cannot yield particles which match the most energetic cosmic rays, and cosmic rays are still of considerable interest because they bring a message about processes taking place in the distant parts of the universe.

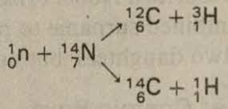
Cosmic rays can also cause problems. Occasionally the sun produces a flare, a sudden outburst of energy which sends an unusually high level of cosmic rays streaming toward the earth. Radio communications can be dis-

Carbon-14 is incorporated into living tissue. When a plant or an animal dies, no new carbon-14 is taken in. This isotope of carbon is radioactive and has a half-life of about 6000 years. One can determine how long ago living material (that includes people and plants) ceased to live (i.e., became mummies or Dead Sea scrolls) by comparing how much carbon-14 is still left in a sample of the material. This use of the carbon-14 isotope is referred to as radiocarbon dating.

rupted and brilliant auroral displays can be seen. Such an outburst represents a very real danger to astronauts, who may be subjected to a heavy bombardment of these energetic little bullets without the protection of the earth's atmosphere.

When primary cosmic ray particles arrive at the earth, they strike atoms and molecules in our atmosphere, setting off a shower of secondary particles, many of which are radioactive. The extremely high energy of most primary particles is diluted in this transfer to a large number of secondary particles. It is the individually less energetic secondary particles which finally reach us on the ground for the most part.

The impact of cosmic rays on the atmosphere produces two important radioisotopes, tritium (^3_1H) and carbon-14 ($^{14}_6C$). Both are produced when cosmic neutrons strike nitrogen atoms (our atmosphere is about 80% nitrogen).



$$^1_0n + ^{14}_7N \rightarrow \begin{cases} ^{12}_6C + ^3_1H \\ ^{14}_6C + ^1_1H \end{cases}$$

3.8 Radiation: How Much Is Too Much?

There are many ways of measuring radiation. A chemist or physicist might wish to know how frequently nuclear disintegrations are occurring within a particular sample. Such nuclear activity is measured in terms of *disintegrations per second* or in *curies* (Ci), named in honor of Marie Curie, the discoverer of radium (section 2.7).

1 Ci = 3.7×10^{10} disintegrations/second (the activity of 1 g of radium)

A source used in the externally applied cobalt radiation treatment of cancer, for example, might be rated at 3000 Ci. For less active samples, metric prefixes are used.

1 millicurie (mCi) = 0.001 Ci = 3.7×10^7 disintegrations/second

A dose of radioactive isotope whose activity is 1 mCi might be taken internally by an adult about to undergo certain types of diagnostic scanning procedures (section 3.14).

1 microcurie (μCi) = 0.000 001 Ci = 3.7×10^4 disintegrations/second

A child would be subjected to a smaller dose, perhaps 10 to 50 μCi for some kinds of diagnostic scanning. Obviously a sample whose activity is measured in microcuries represents far less potential danger than a sample measured in curies.

Most of us are more interested in our *exposure* to radiation than in simply counting disintegrations in some sample of radioactive material. The unit of exposure to gamma rays or X rays is the roentgen (R). Named after Wilhelm Roentgen, who discovered X rays in 1895, a roentgen is defined as the amount of gamma or X rays required to produce ions carrying a total of 2.1 billion units of electrical charge (+ or −) in 1 cm^3 of dry air at 0 °C and normal atmospheric pressure. The definition is a classic of scientific terminology, very precise but probably meaningless to most people. (If you read it over again, you will find in the definition about a half-dozen terms which were introduced in the first two chapters of this book.) The roentgen is a measure of the energy of the beam of rays, indicating how badly an air sample would be disrupted by a particular source of X rays or gamma rays. It is still not quite the unit that relates directly to us. The degree of ionization in tissue is not quite the same as that in air.

What we are really interested in is damage to tissue. The standard unit for *absorbed* dose of ionizing radiation is the *rad* (radiation-absorbed dose). An exposure to 1 rad means that each gram of absorbing tissue has absorbed 100 *ergs* of radiation energy.

$$1 \text{ erg} = 10^{-7} \text{ J} = 2.39 \times 10^{-8} \text{ cal}$$

$$1 \text{ rad} = 100 \text{ ergs absorbed} = 2.39 \times 10^{-6} \text{ cal absorbed}$$

In terms of the amount of heat energy absorbed, the rad is an extremely small unit (1 000 000 rads would be only 2.39 cal). The "absorption" of a diet cola provides perhaps a thousand times that much energy to the body. But it isn't the heat that is dangerous. It is the formation of highly reactive ions (hence the term *ionizing radiation*) and other molecular fragments within the cell that makes radiation so hazardous to us and other living things. In fact, it is estimated that about 500 rads would kill most of us. A single dose of 1000 rads would kill nearly any mammal. For comparison 1 rad is about the average yearly radiation dose absorbed by an individual from medical and dental X rays. A radium dial watch provides perhaps a 1-millirad (mrad) dose of radiation per hour.

There is one other unit for measuring radiation which is worth mentioning. This is the *rem*, which is an acronym for roentgen equivalent in man. It is a measure of the biological damage produced by a particular dose of radiation. Again, there is a precise definition for the rem, but it will probably be useful for us to define the term more generally. A value in rems tells you how the biological damage resulting from exposure to some radiation compares to the damage which would have resulted from a set standard. For example, if a dose of a particular radiation is rated at 4.5 rems, that means that the dose caused the same biological damage as would 4.5 rads of the standard radiation.

These terms are often confusing, particularly the roentgen, the rad, and the rem. It is not critical for you to know how many disintegrations occur in 30 minutes in a 2.7-Ci sample of radium. What you should know is that the number of curies tells you how active the sample is; the number of

For our purposes, we may consider a roentgen and a rad to be about equal. When absorbed in muscle tissue, 1 R will generate about 1 rad of energy.

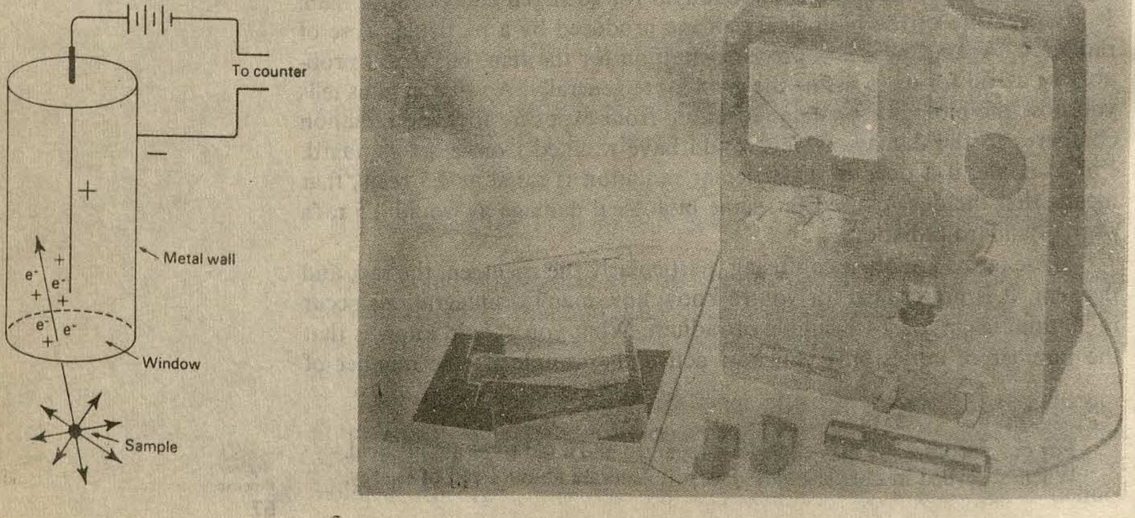
roentgens, how much energy a particular dose transfers to the air; the number of rads, how much energy a dose transfers to tissue; and the number of rems, how much biological damage the dose can accomplish. In all instances, it can be said that, the larger the number, the more potential danger the sample represents.

3.9 Radiation: How Do We Know It Is There?

Generally, we can't see, hear, feel, taste, or smell radiation. Then how do we know that it is there? Most of us have seen or heard of *Geiger counters*. These are instruments that extend our senses so that we can see or hear the effects of radiation. A Geiger counter has a tube with a window at one end (**figure 3.5**). The tube is filled with a gas at low pressure. A wire with a high positive potential (a large excess of positive charge) extends down the center of the tube. Radiation entering the tube will produce ions by knocking electrons off the gas molecules, and the electrons will be attracted to the positively charged wire in the center of the tube. Positive ions will move to the metal wall. A small electrical current, which can be amplified and used to produce a meter reading or a clicking sound or to cause a light to flash, will flow between the two electrodes. The meter can be calibrated in counts per minute or in other convenient units.

Another type of instrument, called a *scintillation counter*, makes use of the fact that tiny flashes of light are produced when radiation strikes certain materials called *phosphors*. (Zinc sulfide is a phosphor. This substance was used to detect radiation in early experiments carried out at the turn of the century.) These phosphors have the ability to convert the kinetic energy of a moving particle to visible light. A device called a *photomultiplier* converts the light output of a scintillator into a pulse of electricity that can be counted automatically.

Figure 3.5 The Geiger counter. (a) Schematic diagram. (b) Photograph. (Photo courtesy of Sargent-Welch Scientific Company, Skokie, Ill.)



Many variations of these basic radiation detectors are available for special purposes. Their functions, though, are the same in principle as the functions of the Geiger counter and the scintillation counter.

Individuals who work with radioactive materials wear personal detectors, simple film badges worn on their pockets or at their waists or as rings. These are not sophisticated electronic devices; instead, they react to radiation as film does to light. A certain dose of radiation will cause the film in the badge to become exposed, alerting the wearer to the potential danger. Individuals working in nuclear power plants or in hospital radiology laboratories use such devices.

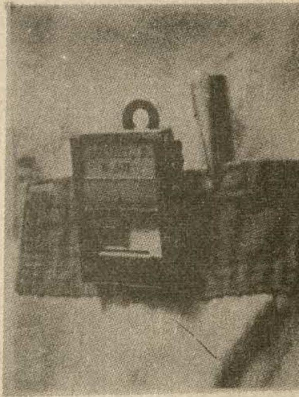


Figure 3.6 Film badges are worn by persons working around radioactive materials. (Reprinted from Asimov, Isaac and Dobzhansky, T., *The Genetic Effects of Radiation*, Oak Ridge, Tehn.: U.S. Energy Research and Development Administration, 1966.)

3.10 Into Each Life Some Radiation . . .

Just sitting there you are getting zapped by all kinds of radiation. There is radiation from natural sources striking us at all times. This *background radiation* is made up of cosmic rays and of radiation from naturally occurring radioisotopes buried in the earth's crust (or in materials derived from this source—the bricks of a house, for example). Background radiation varies from place to place. People who live at high altitudes receive more cosmic radiation. Since air absorbs some of the rays, those who live at low altitudes receive less radiation from this source.

About 50 of the 350 or so natural isotopes are radioactive. The most important of these are potassium-40 ($^{40}_{19}K$), thorium-232 ($^{232}_{90}Th$), and the isotopes of uranium. Gamma rays from potassium-40 and thorium-232 are more significant sources of *external* background radiation, that is, of radiation outside our bodies. Carbon-14 ($^{14}_{6}C$) and tritium ($^{3}_{1}H$), formed in the upper atmosphere by cosmic rays (section 3.8), contribute little to our external exposure, but they are important sources of *internal* background radiation. Carbon and hydrogen are important elements in our bodies, and the radioactive isotopes are incorporated in body tissue along with the more common nonradioactive isotopes. Potassium-40 contributes to internal background radiation also.

We should comment a bit on one characteristic of the various kinds of radiation. It is termed *penetrating power*. All other things being equal, the more massive the particle, the less its penetrating power. Of alpha, beta, and gamma rays, alpha rays are the least penetrating. These are streams of helium nuclei, each particle with a mass number of 4. Beta rays are more penetrating than alpha rays. The electrons which make up the stream of beta particles are assigned a mass number of 0. These particles are not really massless, but they are very much lighter than alpha particles. Gamma rays are a form of high-energy light and are truly massless. These are the most penetrating of the three radiations.

It may seem contrary to common sense that the biggest particles make the least headway. Consider that penetrating power reflects the ability of the radiation to make its way through a sample of matter. It is as if you were trying to roll some rocks through a field of boulders. The alpha particle acts as if it were a boulder itself. Because of its size, it can't get very far before it bumps into and is stopped by the other boulders. The beta particle acts like a small stone. It can sneak between boulders and perhaps

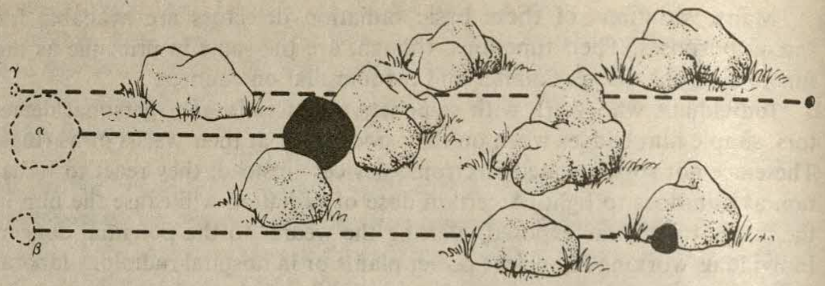


Figure 3.7 Shooting radioactive particles through matter is like rolling rocks through a field of boulders—the larger ones are more easily stopped.

ricochet off one or another until it has made its way further into the field. The gamma ray can be compared to an insect which can get through the smallest openings, and although it may brush against some of the boulders, it can, in general, make its way through most of the field without being stopped.

At the beginning of this discussion we said that, all other things being equal, this is how things worked. But all other things are not always equal. The faster a particle moves or the more energetic the radiation is, the more penetrating power it has. Cosmic rays with very high energy have fantastic penetrating power. Particles which would ordinarily be stopped by the skin can pass right through the body when traveling at the speeds attained by some cosmic ray particles.

Let's get back to particles of equal energy. Which kind does the most damage? In general, the big ones. The big ones don't travel very far, so they dump all of their energy into a small volume of tissue. The small ones have longer paths, and they release their energy all along this path. The effect is diluted over this larger area. Apparently the body can repair some low-level damage. But if a critical molecule comes under massive assault, it may be irreparably damaged, and the body will suffer a permanent effect.

Now we can return to our consideration of background radiation. Radiation from uranium and thorium penetrates air and skin so little that it presents no external threat. Uranium and thorium present serious problems, however, when swallowed or inhaled: they break down to other radioactive elements, including radium. Radium resembles calcium in its chemical properties (if you check the periodic table, you will find that both are Group IIA elements), and it readily replaces calcium in our teeth and bones. Indirectly, then, uranium and thorium contribute to our internal background radiation. The same lack of penetrating power which makes elements relatively innocuous on the outside makes them more significant on the inside. If their radiation is not penetrating, then all of it is trapped within the body, where it destroys vital components of our cells.

So you see that we are being constantly bombarded by radiation. In fact, we ourselves are radioactive. Since people have been exposed to background radiation throughout the course of human evolution, there is evidently little permanent damage to our bodies (or else, whatever damage is done we have come to accept as the normal condition of the body). Some are becoming

Table 3.3
The natural background radiation

Type	*Source*	*Dose Rate (in millirads per year)*	*Varies with*
External	Cosmic rays	30–60	Latitude and altitude
	Soil potassium-40, thorium, uranium	30–100	Location (mineral deposits) and dwelling (least in tents, greatest in stone buildings)
Internal	Thorium, uranium, and decay products	40–400	Location and water supply
	Potassium-40	20	Not very variable
	Carbon-14	2	Not very variable
	Tritium	2	Not very variable
Total		100–600	

Adapted from Frigerio, Norman A., *Your Body and Radiation*, Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1967.

concerned, though, about additional radiation exposure from medical sources, atmospheric testing of nuclear weapons, and nuclear power plants. Most of us get a maximum of 150 mrems of background radiation per year.* We may get an additional 20 to 50 mrems from medical X rays. Fallout varies a great deal. France, China, and India conducted atmospheric tests in 1974. We probably get at most 1.5 mrems from these tests. Radiation released from nuclear power plants in 1970 exposed us to 0.85 mrems of radiation (less than 0.6% of background). As we depend more and more on nuclear power, this last category could increase significantly (see, for example, reference 4).

3.11 Radiation and Living Things

High doses of radiation (on the order of 2000 rads) cause gross destruction of tissue. A person exposed to about 2000 rads passes into shock and dies in a few hours. With exposures of 500 to 1000 rads, the person usually survives long enough to exhibit the several phases (reference 16) of the acute radiation syndrome.

Phase 1: A short latent period (a few hours) when no effects are observed.
Phase 2: A period of nausea and vomiting (which usually end in 24 hours) and of a drop in white blood cell count.

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*Cigarette smokers get a bit more radiation than the rest of us. In fact, Dr. Edward R. Martell, of the National Center for Atmospheric Research, thinks that lung cancer among smokers is caused by radioactive dust. Radon decay products become attached to dust particles. These, he says, are captured by the sticky hairs on tobacco leaves. During smoking, some of these particles are trapped in the bronchi. Alpha emitters among the radon decay products are the main source of damaging radiation. A pack-a-day smoker gets an extra 40 mrems per year.

Phase 3: A period of few symptoms. A low-grade fever may persist.

Phase 4: The last period. Loss of hair begins rather abruptly anywhere from about the 17th through the 21st day. Increased discomfort sets in with loss of appetite and diarrhea. The body temperature rises and the patient complains of pain in the throat and gums. Emaciation sets in, the general condition deteriorates, and the patient dies.

With smaller doses, recovery can take place. Such recovery may not be complete. Malignancy may show up, even years later. And genetic effects may appear in succeeding generations.

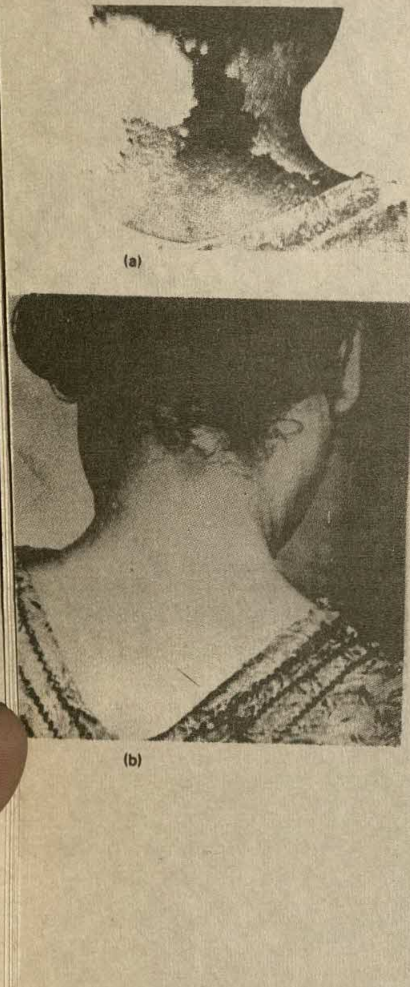


Figure 3.8 Burns from beta rays cause changes in skin pigmentation. (a) The skin 1 month after exposure. (b) The skin upon full recovery, 1 year after exposure. (Reprinted from Frigeria, Norman A., *Your Body and Radiation*, Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1967.)

Some cells are more susceptible to radiation than others. Those that are being constantly and rapidly replaced are affected most. These include the blood cells and those organs responsible for producing blood cells, such as the bone marrow, the intestinal mucosa, germ cells, and embryonic cells. Damage to reproductive cells will show up as abnormalities in the descendants of affected persons.

The effect of radiation varies greatly from species to species. It may even vary a great deal among organisms within a species. To take this variability into account, research workers use a term known as the LD_{50}/30 days. This indicates the dosage required to kill 50% of the individuals in a large group within 30 days. Primitive organisms such as viruses, bacteria, and yeasts have much greater ability to withstand radiation than do mammals (**table 3.4**).

These doses are whole-body exposures. Certain parts of the body can be exposed to much higher doses without death of the subject resulting. For example, while exposure of bone marrow to 500 to 1000 rads will lead to death, a 100 000-rad dose to the arms might be survived. This is not to say that no damage occurs. Indeed, it is very likely that the arm would have to be amputated. However, the functioning of the arm is not as critical to the overall health of the body as the functioning of the bone marrow.

3.12 Radiation and Cancer: Good News, Bad News

Cancer is not one disease but many. Some forms are particularly susceptible to radiation therapy. Radiation is carefully aimed at the cancerous

Table 3.4
LD_{50}/30 days values for various species

Organism	*LD_{50} (in rems)*
Dog	310
Pig	375
Human	400–450 (estimated)
Monkey	600
Rat	790
Yeast	10 000
Bacterium	100 000
Virus	1 000 000

Adapted from Williams, K., Smith, C. L., and Chalke, H. D., *Radiation and Health*, Boston: Little, Brown, 1962.

tissue, and exposure of normal cells is minimized. If the cancer cells are killed by the destructive effects of the radiation, the malignancy is halted. But persons undergoing radiation therapy often get quite sick from the treatment. Nausea and vomiting are the usual symptoms of radiation sickness. (Remember that intestinal mucosa is particularly susceptible to radiation.) Thus, the aim of radiation therapy is to destroy the cancerous cells before too much damage is done to the healthy cells. Radiation is most lethal to rapidly reproducing cells, and this is precisely the characteristic of cancer cells which allows the therapy to be successfully applied.

For many years radium salts were used for the radiation treatment of cancer. Radium-226 is an alpha and gamma emitter.

$$^{226}_{88}\text{Ra} \longrightarrow {}^{222}_{86}\text{Rn} + {}^{4}_{2}\text{He} + {}^{0}_{0}\gamma$$

The radon (Rn) product is a radioactive gas. To prevent its escape, the radium was sealed in tiny hollow needles made of gold or platinum. These could be inserted directly into a tumor and left there to irradiate the surrounding tumor tissue until the desired dosage had been administered. Unfortunately, the needles were so small that they were sometimes lost. Frantic efforts to find them were not always successful.

During recent years, cobalt-60 has come into widespread use. It is easily made by neutron bombardment of ordinary cobalt-59 in certain facilities which specialize in the synthesis of radioisotopes.

$$^{59}_{27}\text{Co} + {}^{1}_{0}\text{n} \longrightarrow {}^{60}_{27}\text{Co}$$

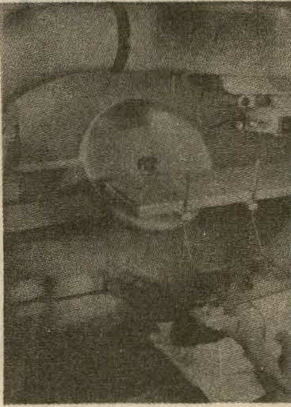
The cobalt-60 emits beta rays and strong gamma rays, but in medical practice the betas are screened out. Cobalt-60 teletherapy units with intensities of over 1000 Ci are now quite common (**figure 3.9**). The radioactive source has a limited life. The half-life of cobalt-60 is 5.3 years. Over a period of time the source will weaken beyond useful limits and have to be replaced. Nevertheless, cobalt-60 is cheaper than radium. Its shorter half-life also means that a given radiation dosage can be achieved with a smaller sample.

Radiation therapy is not without its costs. In addition to sickness, the radiation can cause mutations. Occupational exposure of health professionals may lead to increased birth defects in their children. Indeed, radiation is known to cause some forms of leukemia, a disease of the blood-forming organs.

People working with radioactive materials can do several things to protect themselves. The simplest is to move away from the source, for intensity of radiation decreases as the square of the distance. If the intensity at 1 m is 100 units, it will be only 25 units at 2 m ($1/(2^2)$ or $\frac{1}{4}$ as much). At 3 m, the intensity will be only 11 units ($1/(3^2)$ or $\frac{1}{9}$ as much), and, at 10 m, the radiation intensity will be only 1 unit ($1/(10^2)$ or $\frac{1}{100}$ as much).

Workers can also be protected by shielding. A sheet of paper will stop most alpha particles. A block of wood or a thin sheet of aluminum will stop beta particles. However, it takes several metres of concrete or several centimetres of lead to stop **gamma rays**.

Figure 3.9 A cobalt-60 unit for radiation therapy. Blocks of tungsten or lead are placed on the diaphragm above the patient's chest to absorb gamma rays and thus focus the treatment on the malignancy. (Reprinted from Phelan, Earl W., *Radioisotopes in Medicine*, Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1966.)



You may recall Rutherford's experiment which led to his proposing the nuclear atom. He fired alpha particles at a sheet of gold foil. Most went straight through. Wait a minute, you say. How can this be so if a sheet of plain old paper will stop most alpha particles? Aha! You get two points for being on your toes. (If you did not wonder about this, return to Go.) A piece of gold foil about two thousand atoms thick, believe it or not, is very, very thin (about 0.002 mm). An ordinary sheet of paper is perhaps a hundred times as thick as that and will stop all but the most energetic alpha particles.

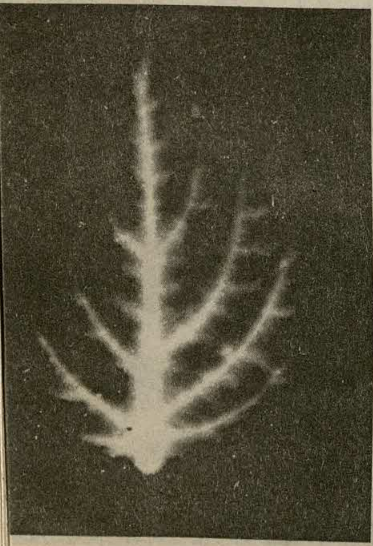
Hospital patients who have ingested therapeutic doses of radioisotopes (but not those who have been treated with an external source) must themselves be regarded as sources of radiation while the radioisotope maintains significant activity. Health personnel who can expect to be exposed to many such patients during their careers must exercise caution in order to avoid exposing themselves to a damaging dose of radiation over a long period.

3.13 Nuclear Sleuths: Radioactive Tracers

Scientists in a wide variety of fields make use of radioisotopes as "tracers" in physical, chemical, and biological systems. Isotopes of a given element, whether radioactive or not, behave nearly identically in chemical and physical processes. Since radioactive isotopes are easily detected, it is relatively easy to trace their movement, even through a complicated system.

As a simple example, let us consider the flow of a liquid through a pipe. Suppose there was a leak in a pipe buried beneath a concrete floor. One could locate the leak by digging up extensive areas of the floor. Or one could add a small amount of radioactive material and trace the flow of liquid with a Geiger counter. Once the leak had been located, only a small area of the floor would need to be dug up for the leak to be repaired. Short-lived isotopes, which disappear soon after doing their job, are usually employed for such purposes.

Figure 3.10 Autoradiograph showing the uptake of phosphorus in a plant. (Reprinted from Comer, C. L., *Fallout*, Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1966.)



In a similar manner, one could trace the uptake of phosphorus by a plant. The plant might be fed some fertilizer containing radioactive phosphorus. A simple method of detection would involve placing the plant on photographic film. Radiation from the phosphorus isotopes would expose the film, much as light would. (The film badges previously mentioned in connection with the detection of radiation are based on this principle. In fact, the original discovery of radioactivity by Becquerel resulted from an unexpectedly exposed film.) The picture produced by the radioactive plant would be called an autoradiograph, and it would show the distribution of phosphorus in the plant (**figure 3.10**).

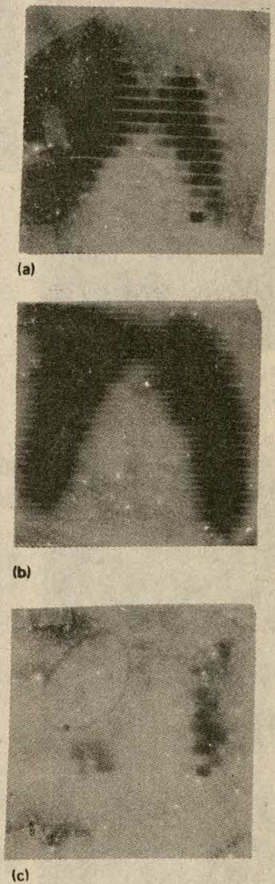
Radioisotopes can also be used to trace the pathways of complicated chemical and biochemical reactions. Perhaps their most important applications, however, have been in the field of medicine.

3.14 Nuclear Tools in Medical Diagnosis

We have spoken of the therapeutic uses of radioisotopes, uses intended to treat or cure a disease. Radioisotopes are also used for diagnostic purposes, to help provide information about the type or extent of illness.

Radioactive iodine-131 ($^{131}_{53}I$) is used to determine the size, shape, and activity of the thyroid gland (**figure 3.11**) as well as to treat cancer located in this gland and to control a hyperactive thyroid. One merely needs to drink some potassium iodide containing iodine-131. The body concentrates iodide in the thyroid. Large doses are used for treatment of thyroid cancer; the radiation from the isotope concentrates in the thyroid cancer cells even if the cancer has spread to other parts of the body. For diagnostic purposes, however, only a small amount is needed. Again the material is concentrated in the thyroid. A detector is set up so that readings are translated into a permanent visual record showing the differential uptake of the isotope. The "picture" which results is referred to as a *photoscan.*

Figure 3.11 A linear photoscanner produced these pictures of (a) a normal thyroid, (b) an enlarged thyroid, and (c) a cancerous thyroid. (Reprinted from Comer, C. L., *Fallout,* Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1966.)



Brain tumors tend to absorb certain ions. For this reason, arsenic-74 ($^{74}_{33}As$), in ionic form, can be used in the detection of these growths. Arsenic-74 is a positron (${}^{0}_{1+}e$) emitter.

$$^{74}_{33}As \longrightarrow {}^{0}_{1+}e + {}^{74}_{32}Ge$$

When a positron encounters an electron (in any ordinary matter there are numerous electrons), two gamma rays are produced.

$${}^{0}_{1+}e + {}^{0}_{1-}e \longrightarrow 2\gamma$$

These travel in exactly opposite directions. Detectors can be placed on opposite sides of the patient's head (**figure 3.12**). When each detector simultaneously "sees" a gamma ray, a count is made. By setting of the recorders so that two simultaneous gamma rays (both produced in the annihilation of the positron and electron) must be seen to be recorded, gamma rays resulting from natural background radiation will be ignored. The tumor can thus be precisely located.

Several types of cancers concentrate phosphate ions to a much greater extent than does surrounding healthy tissue. Therefore, phosphate labeled with $^{32}_{15}P$ can be used to detect these cancer cells. Since phosphorus-32 emits only beta particles, which have relatively low penetrating power, the detector must be placed very close to the suspect cells.

$$^{32}_{15}P \longrightarrow {}^{0}_{1-}e + {}^{32}_{16}S$$

This limits the use of this method to diagnosis of skin cancer and cancer of tissue exposed by surgery.

Sodium-24 is used to detect constriction or obstruction in blood vessels. A little salt (sodium chloride) containing sodium-24 ($^{24}_{11}Na$) ions is injected into a vein in an arm or leg. A counter is used to detect the arrival of the radioisotope in another part of the body. The time it takes to get there tells whether or not there are obstructions in the circulatory system.

For diagnostic scanning, one could imagine an ideal isotope. The isotope would be a gamma emitter. For scanning one wishes to detect radiation outside the body and therefore desires a radiation that can escape from the body, that is, one which has good penetrating power. It would be best if neither alpha nor beta particles were emitted. These are not needed for detection and would simply do unnecessary damage to the body. The gamma rays should be just the right energy. Not so weak that we would have to wait around forever to get enough of a response from our detector, not so strong that they would impart unnecessary energy to the body in making their way out. The half-life should be just right. Not so short that the activity is gone before we can measure it, not so long that significant activity remains long after we have finished our studies.

Happily there is available an isotope very much like this. It is technetium-99^m ($^{99}_{43}Tc^m$). The *m* stands for *metastable,* which means that this isotope will give up some energy to become a more stable version of the same isotope (same atomic number, same atomic weight). The energy it gives up is the gamma ray we need for detecting the isotope while scanning.

$$^{99}_{43}\mathrm{Tc}^m \longrightarrow {}^{99}_{43}\mathrm{Tc} + \gamma$$

The energy of the gamma ray is just about right, and so is the half-life, about 6 hours. With this short a half-life, one must carefully plan one's use of the isotope. In fact, the isotope itself is not what is purchased. The technetium-99^m is formed by the decay of molybdenum-99.

$$^{99}_{42}\mathrm{Mo} \longrightarrow {}^{99}_{43}\mathrm{Tc}^m + {}^{0}_{-1}e + \gamma$$

A container of this molybdenum isotope is obtained, and the decay product, technetium-99^m, is "milked" from the container as needed.

Much effort has gone into making technetium-99^m available in a variety of preparations. In some forms it is useful for kidney scanning; in other

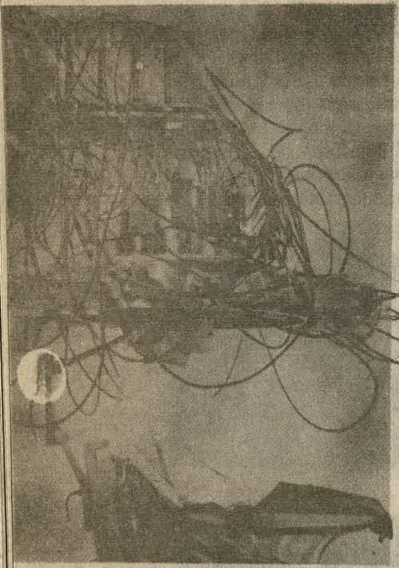


Figure 3.12 This detector uses positron-emitting isotopes to locate brain tumors. (Reprinted from Phelan, Earl W., *Radioisotopes in Medicine,* Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1966.)

Table 3.5
Some radioisotopes and their application in medicine

Isotope	*Name*	*Use(s)*
^{74}As	Arsenic-74	Location of brain tumors
^{51}Cr	Chromium-51	Determination of volume of red blood cells and total blood volume
^{58}Co	Cobalt-58	Determination of uptake of vitamin B_{12}
^{60}Co	Cobalt-60	Radiation treatment of cancer
^{131}I	Iodine-131	Detection of thyroid malfunction; measurement of liver activity and fat metabolism; treatment of thyroid cancer
^{59}Fe	Iron-59	Measurement of rate of formation and lifetime of red blood cells
^{32}P	Phosphorus-32	Detection of skin cancer or cancer of tissue exposed by surgery
^{226}Ra	Radium-226	Radiation therapy for cancer
^{24}Na	Sodium-24	Detection of constrictions and obstructions in the circulatory system
$^{99}Tc^*$	Technetium-99^m	A number of diagnostic uses (see pp. 66–67)
^{3}H	Tritium	Determination of total body water

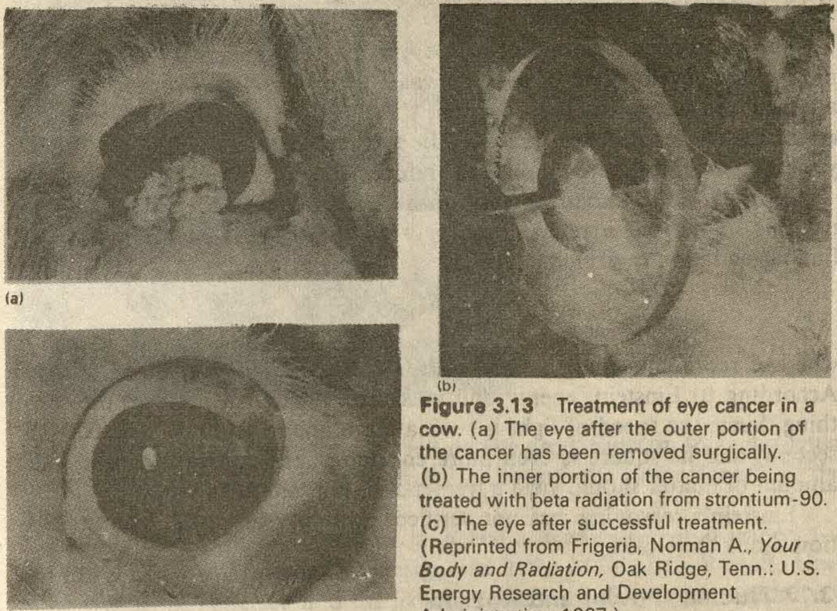


Figure 3.13 Treatment of eye cancer in a cow. (a) The eye after the outer portion of the cancer has been removed surgically. (b) The inner portion of the cancer being treated with beta radiation from strontium-90. (c) The eye after successful treatment. (Reprinted from Frigeria, Norman A., *Your Body and Radiation,* Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1967.)

forms it will be concentrated by the liver and spleen. It can be used for brain scans or for lung scans. Thus, this isotope can replace a number of less than ideal radioisotopes.

Radioisotopes are also widely used to determine the mechanism of drug action. Drug molecules are "tagged" with radioactive atoms. These can be traced through the complex biochemical processes that occur when a drug is metabolized.

Table 3.5 offers a listing of some of the radioisotopes in common use in medicine. The list is necessarily quite incomplete.

3.15 Radioisotopes and Animals and Vegetables

Radioisotopes are also used in veterinary medicine for both therapeutic and diagnostic purposes (**figure 3.13**).

The irradiation of foodstuffs as a method of preservation is also being intensively studied. Such methods can be used to prevent food spoilage because they destroy microorganisms that cause such spoilage. The food so treated shows little change in taste or appearance (**figure 3.14**). The process is not yet in commercial use, but extensive testing is currently being carried out to establish that the products of such treatment are not harmful to human beings.

In the meantime, radioactive tracers are put to good use in agricultural research. They are used to study the effectiveness of fertilizers and weed killers, to compare the nutritional value of various feeds, and to determine the best methods for controlling insects. The purposeful mutation of plants by irradiation has produced new and improved strains of commercially valuable crop plants ranging from tobacco to peanuts.

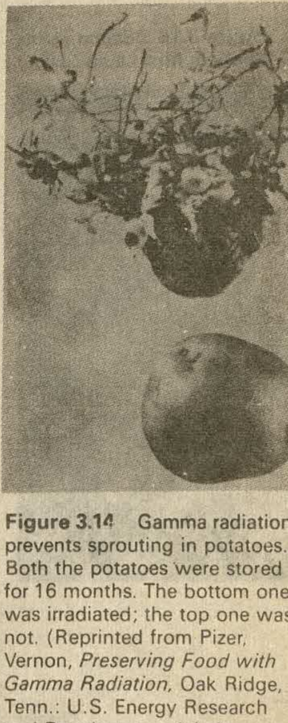


Figure 3.14 Gamma radiation prevents sprouting in potatoes. Both the potatoes were stored for 16 months. The bottom one was irradiated; the top one was not. (Reprinted from Pizer, Vernon, *Preserving Food with Gamma Radiation,* Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1970.)

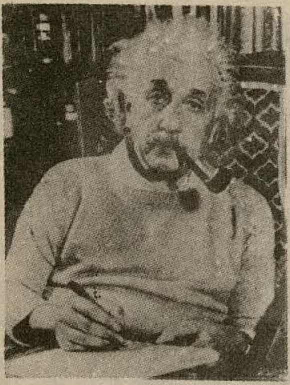


Figure 3.15 Albert Einstein. (Courtesy of Matheson Gas Products, East Rutherford, N.J.)

3.16 Einstein's Equation

Let us return to our study of the history of radioactivity. Perhaps the most noted development of our age was a theoretical one, worked out with a pencil and note pad. These are not the tools one usually associates with a scientist. Albert Einstein may well be the best-known scientist of all time, yet his achievements are those of the mind, not the laboratory.

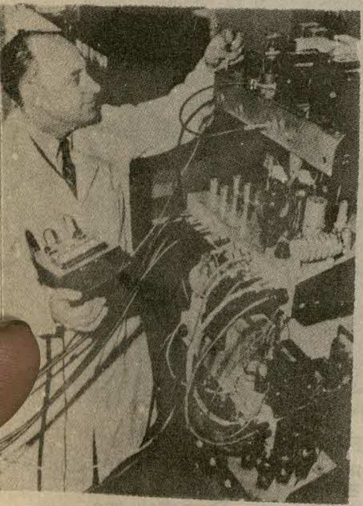
By 1905, Einstein had worked out his special theory of relativity. In doing this he derived a relationship between matter and energy. The now-famous equation is written

$$E = mc^2$$

where E represents energy, m represents mass, and c is the speed of light. According to Einstein, energy and mass are different aspects of the same thing. Since the speed of light is such a large quantity (30 000 000 000 cm/second) and its square is even more enormous, the conversion of a small amount of matter should yield a tremendous amount of energy.*

Einstein's reasoning was not verified until 40 years later. The verification shook the world.

Figure 3.16 Enrico Fermi. (Courtesy of Mrs. Laura Fermi.)



3.17 Nuclear Power and Nazism

A group of physicists headed by the Italian Enrico Fermi was first to study the bombardment of uranium with neutrons, but they failed to interpret their work properly. The German chemists Otto Hahn and Fritz Strassman first correctly interpreted the experiments after discovering that the reaction products were much lighter elements than uranium and included barium (Ba), lanthanum (La), and cerium (Ce). The uranium atom had been split! In this reaction, it wasn't a matter of a small piece (an alpha or a beta particle, for example) being chipped from the original nucleus. Here the nucleus was cleaved, split into two major fragments. Lise Meitner and Otto Frisch calculated the energy associated with the *fission* of uranium and found it to be several times greater than that of any previously known nuclear reaction. In addition, the splitting of the nucleus into two major fragments was accompanied by the release of some smaller fragments, more neutrons. The neutrons thus produced could split other uranium atoms, producing enormous amounts of energy in a chain of reactions (**figure 3.18**).

In 1938, Nazi Germany invaded and annexed Austria. Lise Meitner, an Austrian Jew, fled to Sweden. There she released the news of these momentous discoveries. This news was carried to the United States by Niels Bohr, the Danish physicist who is so well known for his quantum theory of the electronic structure of atoms. Fermi, who had fled Italy to the United States

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*The actual magnitude of the energy depends upon the units used. If the mass is expressed in *grams* and the speed of light in *centimetres per second*, the energy is expressed in *ergs*. The energy equivalent to 1 g of matter is 9×10^{20} ergs, or 90 000 000 000 Btu (British thermal units). This is enough energy to heat the average home for a thousand years (reference 10).

Figure 3.17 Lise Meitner and Otto Hahn in Hahn's laboratory. (Reprinted with permission from Holton, G. J., and Roller, D. H., *Foundations of Modern Physical Science,* Reading, Mass.: Addison-Wesley, 1958. Copyright © 1958 by Addison-Wesley Publishing Company.)

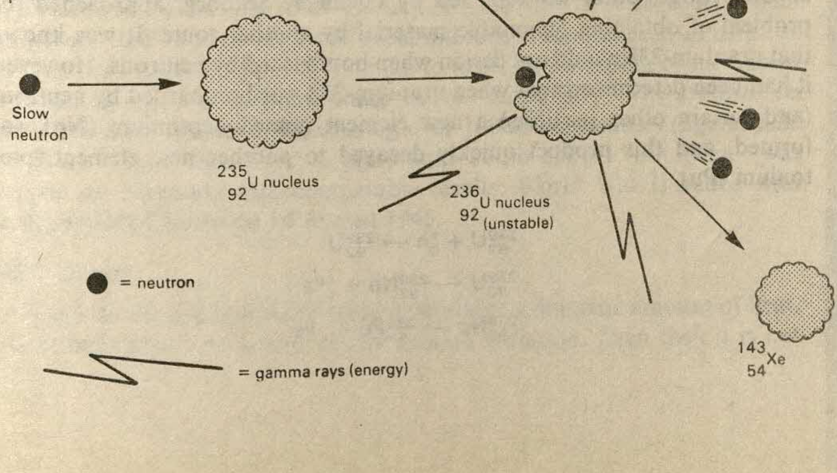
because his wife was Jewish, prevailed on the great Einstein to sign a letter to President Franklin D. Roosevelt indicating the importance of the discovery.

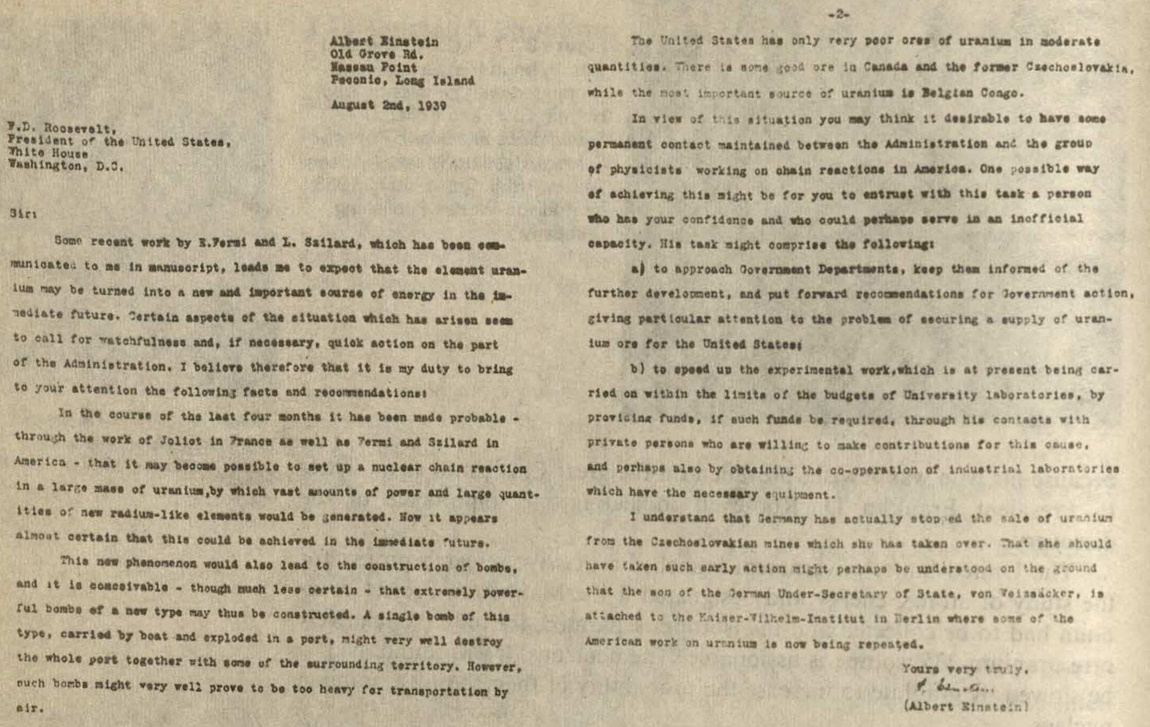
The United States government launched a massive research project for the study of atomic energy and designated it the Manhattan Project. Uranium had to be collected and the isotopes separated, for only the relatively rare uranium-235 isotope is fissionable. The neutrons, it was found, had to be slowed by graphite to increase the probability of their hitting a uranium nucleus.

Fermi and his group achieved the first sustained nuclear reaction on 2 December 1942 under the bleachers at Stagg Field of the University of Chicago.

Separation of the uranium-235 isotope from the more abundant uranium-238 proceeded very slowly at a top secret installation at Oak Ridge, Ten-

Figure 3.18 The splitting of a uranium atom. The neutrons produced in this fission can split other uranium atoms, thus sustaining a chain reaction. The splitting of one uranium-235 atom yields 8.9×10^{-18} kilowatt-hours (kwh) of energy. Fission of a mole of uranium-235 (6.02×10^{23} atoms) produces 5 300 000 kwh of energy.





Albert Einstein
Old Grove Rd.
Nassau Point
Peconic, Long Island

August 2nd, 1939

F.D. Roosevelt,
President of the United States,
White House
Washington, D.C.

Sir:

Some recent work by E.Fermi and L. Szilard, which has been communicated to me in manuscript, leads me to expect that the element uranium may be turned into a new and important source of energy in the immediate future. Certain aspects of the situation which has arisen seem to call for watchfulness and, if necessary, quick action on the part of the Administration. I believe therefore that it is my duty to bring to your attention the following facts and recommendations:

In the course of the last four months it has been made probable - through the work of Joliot in France as well as Fermi and Szilard in America - that it may become possible to set up a nuclear chain reaction in a large mass of uranium,by which vast amounts of power and large quantities of new radium-like elements would be generated. Now it appears almost certain that this could be achieved in the immediate future.

This new phenomenon would also lead to the construction of bombs, and it is conceivable - though much less certain - that extremely powerful bombs of a new type may thus be constructed. A single bomb of this type, carried by boat and exploded in a port, might very well destroy the whole port together with some of the surrounding territory. However, such bombs might very well prove to be too heavy for transportation by air.

-2-

The United States has only very poor ores of uranium in moderate quantities. There is some good ore in Canada and the former Czechoslovakia, while the most important source of uranium is Belgian Congo.

In view of this situation you may think it desirable to have some permanent contact maintained between the Administration and the group of physicists working on chain reactions in America. One possible way of achieving this might be for you to entrust with this task a person who has your confidence and who could perhaps serve in an inofficial capacity. His task might comprise the following:

a) to approach Government Departments, keep them informed of the further development, and put forward recommendations for Government action, giving particular attention to the problem of securing a supply of uranium ore for the United States;

b) to speed up the experimental work,which is at present being carried on within the limits of the budgets of University laboratories, by providing funds, if such funds be required, through his contacts with private persons who are willing to make contributions for this cause, and perhaps also by obtaining the co-operation of industrial laboratories which have the necessary equipment.

I understand that Germany has actually stopped the sale of uranium from the Czechoslovakian mines which she has taken over. That she should have taken such early action might perhaps be understood on the ground that the son of the German Under-Secretary of State, von Weizsäcker, is attached to the Kaiser-Wilhelm-Institut in Berlin where some of the American work on uranium is now being repeated.

Yours very truly.

(Albert Einstein)

Figure 3.19 This letter from Albert Einstein to Franklin Roosevelt led to the development of the first atomic bomb. (Reprinted from Asimov, Isaac, *Worlds within Worlds,* Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1972.)

nessee. This separation could not be done by chemical reaction, for the isotopes behave identically chemically. Separation was accomplished by conversion of all the uranium to the gas uranium hexafluoride. Molecules of the latter containing the uranium-235 isotope are slightly lighter and move slightly more rapidly than those molecules containing the uranium-238 isotope. The gaseous uranium hexafluoride was allowed to pass through thousands of consecutive pinholes, a process in which the molecules that contained uranium-235 gradually outdistanced the others. The scientists eventually obtained 15 kg of the separated uranium-235 isotope, enough to make a small explosive device.

While the tedious work of separating uranium isotopes was under way at Oak Ridge, other workers, led by Glenn T. Seaborg, approached the problem of obtaining fissionable material by another route. It was known that uranium-238 would not fission when bombarded by neutrons. However, it had been determined that when uranium-238 was bombarded by neutrons (and certain other particles) a new element named neptunium (Np) was formed, and this product quickly decayed to another new element, plutonium (Pu).

$$^{238}_{92}\mathrm{U} + {}^{1}_{0}\mathrm{n} \longrightarrow {}^{239}_{92}\mathrm{U}$$

$$^{239}_{92}\mathrm{U} \longrightarrow {}^{239}_{93}\mathrm{Np} + {}_{-1}^{\;\,0}\mathrm{e}$$

$$^{239}_{93}\mathrm{Np} \longrightarrow {}^{239}_{94}\mathrm{Pu} + {}_{-1}^{\;\,0}\mathrm{e}$$

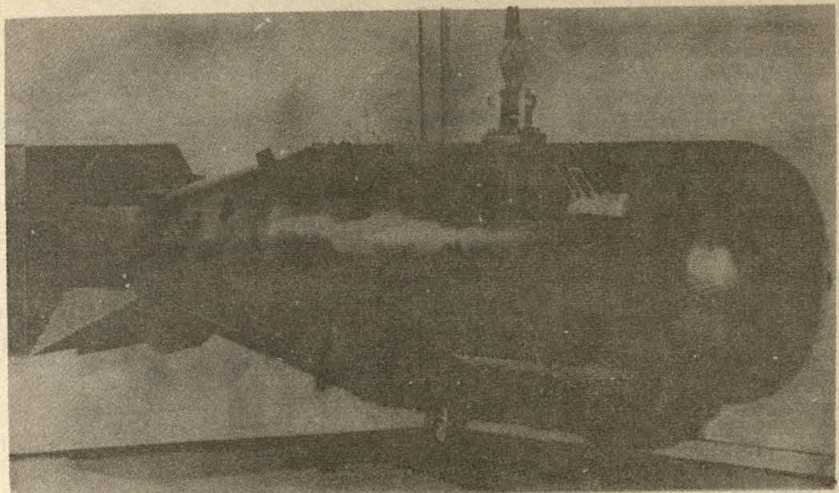


Figure 3.20 Nuclear bomb of the type exploded over Hiroshima. The diameter of the bomb is 71 cm, and its length is 305 cm. It weighs 4.1 t and has explosive power equivalent to about 18 000 t of TNT. (Smithsonian Institution, Washington, D.C.)

One isotope of plutonium, plutonium-239, was found to be fissionable and, thus, was suitable material for the making of a bomb. A series of large reactors were built near Hanford, Washington, for the making of plutonium.

Before a fissionable material can sustain a chain reaction, a certain minimum amount, called the *critical mass,* must be brought together. There must be enough fissionable nuclei that the neutrons released in one fission process will have a good chance of finding another fissionable nucleus before escaping from the mass.

By July 1945 enough plutonium had been made for a bomb to be assembled. This first atomic bomb was tested in the desert near Alamogordo, New Mexico, on 16 July 1945. The heat from the explosion vaporized the 30-m (100-ft) steel tower on which it was placed and melted the sand for several acres around the site. The light released was the brightest anyone had ever seen.

Figure 3.21 The now-familiar mushroom cloud that follows an atomic explosion. (Courtesy of Encyclopaedia Britannica, Inc., Chicago.)

Some of the scientists were so awed by the force of the blast that they argued against its use on Japan. A few, led by Leo Szilard, argued for a demonstration of its power at an uninhabited site. But fear of a well-publicized "dud" and the desire to avoid millions of casualties in an invasion of Japan led President Harry S. Truman to order the dropping of the bombs on Japanese cities. A uranium bomb called "Little Boy" was dropped on Hiroshima on 6 August 1945, causing over 100 000 casualities (**figures 3.20** and **3.21**). Three days later, a plutonium bomb called "Fat Man" was dropped on Nagasaki with comparable results. World War II ended with the surrender of Japan on 14 August 1945.

3.18 Fallout

When the atomic bomb explodes, it produces a fantastic amount of heat, devastating shock waves, and deadly gamma radiation. Even then it is not

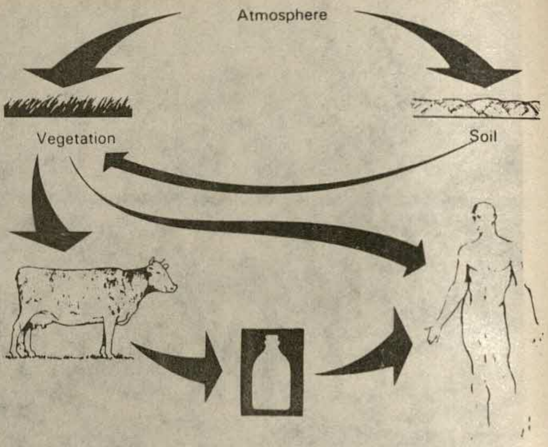


Figure 3.22 Pathways of strontium-90 from fallout. (Reprinted from Comer, C. L., *Fallout*, Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1966.)

through, for the products of uranium fission are radioactive. These materials may rain upon parts of the earth even thousands of miles away, days and weeks later.

A typical fission reaction (see **figure 3.18**) might be

$${}^{235}_{92}\mathrm{U} + {}^{1}_{0}\mathrm{n} \longrightarrow {}^{90}_{38}\mathrm{Sr} + {}^{143}_{54}\mathrm{Xe} + 3\,{}^{1}_{0}\mathrm{n}$$

The neutrons may strike additional uranium atoms, carrying on the chain reaction. The strontium (Sr) and xenon (Xe) atoms are radioactive and are a part of the fallout.

The uranium atom can split in 40 or more ways, producing 80 or 90 primary radioactive products. Some of these produce radioactive *daughter* isotopes. For example, xenon-143 undergoes beta decay, with a half-life of 1 second.

$${}^{143}_{54}\mathrm{Xe} \longrightarrow {}^{0}_{1-}\mathrm{e} + {}^{143}_{55}\mathrm{Cs}$$

The cesium isotope is also radioactive—as are its daughters, and their daughters. Still other radioisotopes, such as carbon-14 and tritium, are formed by the impact of neutrons produced in the explosion on molecules of the atmosphere. Thus, fallout is exceedingly complex. We will consider only a few of the more important isotopes.

Of all the isotopes, strontium-90 presents the greatest hazard to people. This isotope has a half-life of 28 years. Strontium-90 reaches us primarily through milk and vegetables (**figure 3.22**). Because of its similarity to calcium (both are Group IIA elements), strontium-90 is incorporated into bone. There it remains a source of internal radiation for many years.

Although strontium-90 is a greater long-term hazard, iodine-131 may present a greater threat immediately after a nuclear explosion. The half-life of iodine-131 is only 8 days, but it is produced in relatively large amounts. Iodine-131 is efficiently carried through the food chain (**figure 3.23**). In the body it is concentrated in a small area, the thyroid gland. It is precisely this characteristic that makes this same isotope so useful for diagnostic scanning.

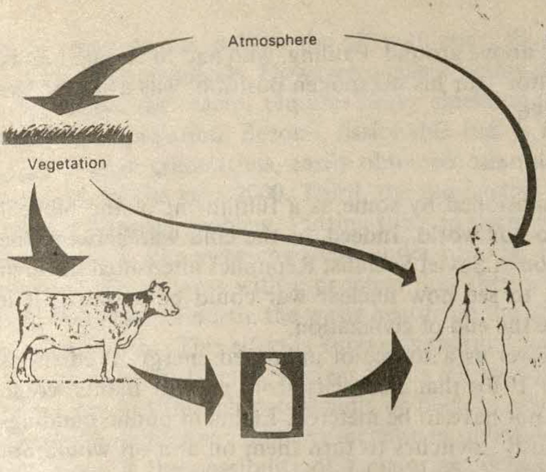


Figure 3.23 Pathways of iodine-131 from fallout. (Reprinted from Comer, C. L., *Fallout*, Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1966.)

However, for a healthy individual, the incorporation of radioactive iodine in the thyroid gland offers no useful information, only damaging side effects.

Another important isotope in fallout is cesium-137. Cesium is similar to potassium (both are Group IA elements), and it mimics potassium in the body. Cesium-137 is a gamma emitter and has a half-life of 30 years. It is less of a threat than strontium-90, though, because it is removed from the body more readily. We get cesium-137 through vegetables, milk, and meat (**figure 3.24**).

By the late 1950s, radioactive isotopes from atmospheric testing of nuclear weapons had been detected. Concern over radiation damage from nuclear fallout led to a movement to ban atmospheric testing. Many scientists were leaders in the movement. Linus Pauling, who won the Nobel Prize in chemistry in 1954 for his work in determining the structure of proteins, was a particularly articulate advocate of banning the bomb. In 1963 a nuclear test ban treaty was signed by the major powers—with the exception of France and the People's Republic of China, who continue aboveground tests. Since the signing of the treaty, India has joined the nuclear

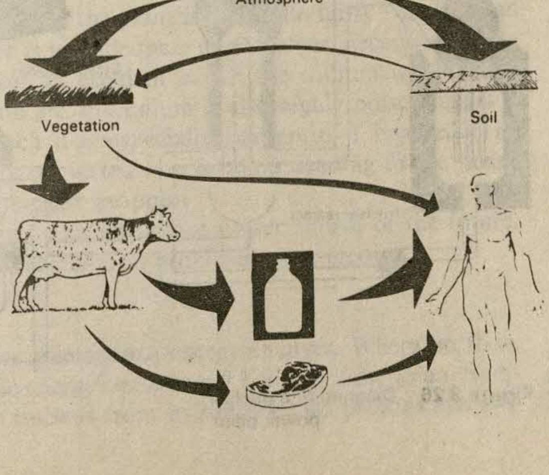


Figure 3.24 Pathways of cesium-137 from fallout. (Reprinted from Comer, C. L., *Fallout*, Oak Ridge, Tenn.: U.S. Energy Research and Development Administration, 1966.)

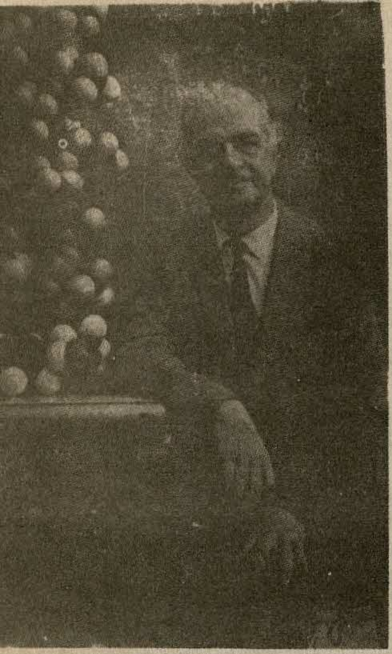


Figure 3.25 Linus Pauling, winner of two Nobel Prizes.

club, by exploding a bomb above ground. Pauling, who had to endure taunts of "communist" and "traitor" for his outspoken position, was awarded the Nobel Prize for peace in 1962.

3.19 Nuclear Power Plants

Nuclear power was envisioned by some as a fulfillment of the biblical prophecy of a fiery end to our world. Indeed, as the cold war between the United States and the Union of Soviet Socialist Republics intensified through the 1950s, it was difficult to see how nuclear war could be avoided. If it came, it could very well be the end of civilization.

Others saw nuclear power as a source of unlimited energy. Predictions were common in the later 1940s that electricity from nuclear plants would be so cheap that it would not have to be metered. Lights in public buildings could be left on continuously; switches to turn them on and off would not be needed! Obviously, such predictions have not come true: we are now confronted with an energy crisis. Let's take a look at nuclear power plants to see why such facilities have not yet lived up to their promise of plentiful power.

Nuclear power plants use the same fission reactions as nuclear bombs. The reaction is controlled, though, by the insertion of boron steel or cadmium control rods. Boron (B) and cadmium (Cd) absorb neutrons readily, thus preventing the neutrons from participating in the chain reaction. These rods are installed as the reactor is built. Removing them part way starts the chain reaction; the reaction is stopped if the rods are pushed all the way in.

The tremendous heat of the nuclear reaction is used to produce steam. The steam is used to turn turbines, which generate electricity (**figure 3.26**). Nuclear power plants have one great advantage over coal- and oil-burning

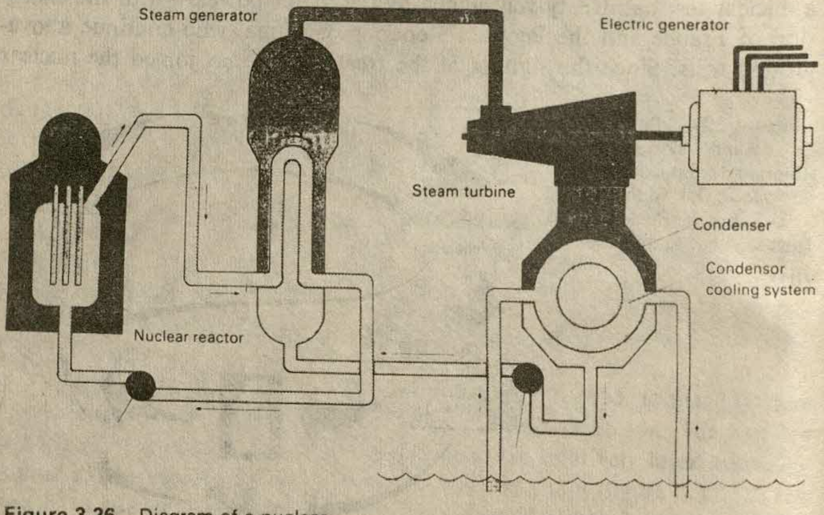


Figure 3.26 Diagram of a nuclear power plant.

plants—they do not pollute the air with soot, fly ash, sulfur dioxide, and other noxious chemicals. However, nuclear plants offer some disadvantages as well. First, the reactor requires heavy shielding to protect operating personnel from radiation. Second, fissionable fuel is rare and expensive. The supply of high-grade (thus, easily obtained) uranium ore will run out, it is estimated, by the year 2000. Third, the radioactive fission products present a serious disposal problem. Putting them in deep wells or mines or burying them at sea is like sweeping them under the rug. Do we have the right to leave our descendants with a problem that they will have to contend with for 10 000 years? Fourth, the waste heat from the generating plants heats up the environment. This effect is known as thermal pollution. Fifth, no matter how carefully constructed, nuclear plants release some radioactivity into the environment. Although proponents of nuclear power say that the amount is negligible, others say that *any* increase in radiation exposure is dangerous. Sixth, there is the possibility of a major accident (although nuclear explosions are *not* possible) at a reactor site. Such an accident would release large amounts of radioactivity to the surrounding areas.

There is considerable controversy over most of these points, and scientists stand on each side. While they may be able to agree on the results of laboratory experiments, scientists obviously do not agree on what is best for society. Those who wish to explore this controversy further are urged to see the references and readings at the end of this chapter.

3.20 Breeder Reactors

Less than 1% of naturally occurring uranium is the fissionable uranium-235 isotope. Large quantities of uranium-238 are available as a by-product of the production of uranium-235. We have seen how uranium-238 can be converted to fissionable plutonium-239 by bombardment with neutrons. A reactor can be built with a core of fissionable plutonium surrounded by uranium-238. As the plutonium fissions, neutrons convert the uranium-238 "shield" to more plutonium; the reactor "breeds" more fuel than it consumes. There is enough uranium-238 to last several centuries, so one of the disadvantages listed for nuclear plants is thereby overcome.

Breeder reactors have some problems of their own, however. Plutonium is fairly low melting (640 °C), and the plant is limited to fairly "cool"—and inefficient—operation. Water is not adequate as a coolant, necessitating the use of liquid sodium. Should an accident occur, the sodium would react violently with both water and air. Plutonium is also highly poisonous. It is an alpha emitter, and as such it is especially dangerous if ingested. The plutonium can also be easily converted into a bomb, leading to the possibility of a further spread of nuclear weapons.

The breeder reactor may be an important power source of the future, but not before some substantial technical problems are overcome.

3.21 Binding Energy

Nuclear reactions involve tremendous energy changes. Where do these enormous amounts of atomic energy come from? Let's consider as an example the building of a helium nucleus from its parts. If two protons and two

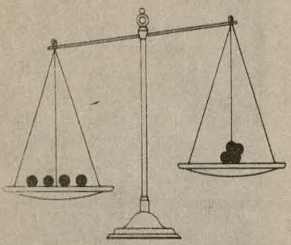


Figure 3.27 Binding energy or mass defect. A helium nucleus weighs *less* than the two protons and two neutrons from which it is made.

neutrons are put together to form a helium nucleus, it should have a mass of 4.031882 amu.

Two protons weigh 2 × 1.007276 = 2.014552 amu
Two neutrons weigh 2 × 1.008665 = 2.017330 amu
Total mass = 4.031882 amu

The actual mass of the helium nucleus is 4.001506 amu. The missing mass, called the *mass defect* or *binding energy*, is 0.030376 amu. Binding energy is energy which the nucleus *doesn't* have. It is the energy given up when the nucleus forms. The larger the binding energy, the more stable the nucleus, or, to put it badly, the happier the nucleus.

Remembering Einstein's $E = mc^2$, we see that this small amount of mass is equivalent to a large amount of energy. If one calculates the binding energy for all the elements, as was done above for helium, and plots a graph using the resulting values, one obtains a curve like that in **figure 3.28.** The most stable nuclei, those with the highest binding energy, are in the vicinity of iron (whose atomic number is 26). The splitting of very large nuclei, like those of uranium atoms, produces smaller daughter nuclei, which are more stable; consequently this splitting releases a lot of energy.

One can also see from the graph that even more energy would be produced if very small nuclei (such as hydrogen nuclei) were combined to form larger, more stable nuclei. This sort of nuclear *fusion* occurs in the explosion of a hydrogen bomb.

3.22 Thermonuclear Reactions

The source of nearly all our energy on earth is the thermonuclear reaction taking place in the sun. Intense temperatures in the center of the sun

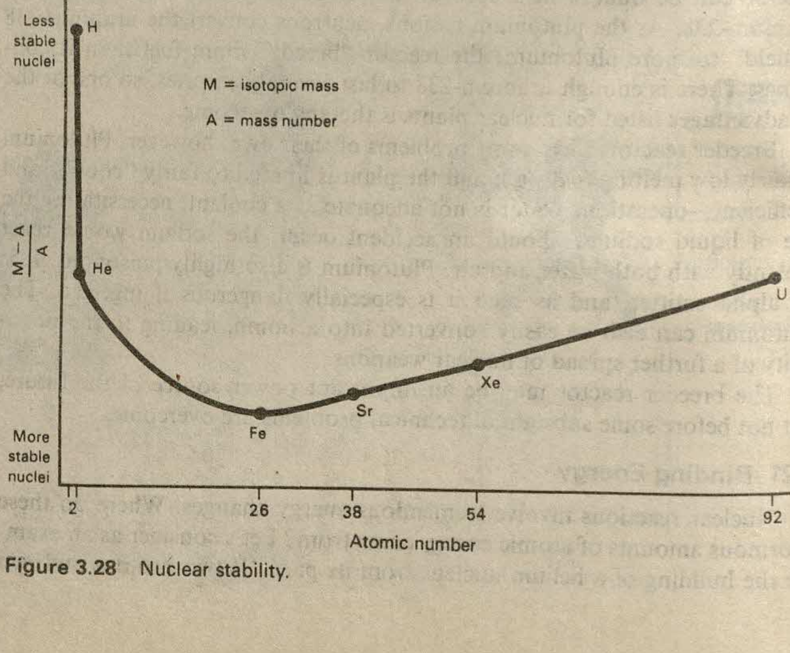


Figure 3.28 Nuclear stability.

cause nuclei to fuse, releasing tremendous amounts of energy. The principal net reaction is believed to be the fusion of four hydrogen nuclei to produce one helium nucleus.

$$4\,{}^{1}_{1}H \longrightarrow {}^{4}_{2}He + 2\,{}^{\ 0}_{1+}e$$

Upon fusion, 1 g of hydrogen releases an amount of energy equivalent to that released by the burning of 17 000 kg (nearly 20 tons) of coal.

The hydrogen bomb makes use of a uranium or plutonium (fission) bomb to provide the tremendous heat necessary to start the nuclei fusing. Extremely high temperatures are required because the nuclei must be moving at great speeds in order to fuse. If they are moving too slowly, the repulsive force experienced by the two like-charged nuclei as they approach one another will prevent them from getting close enough to fuse. In a fission reaction, neutral particles (neutrons) trigger the splitting of the nuclei; therefore, high temperatures are not necessary to initiate the fission reaction.

Even at the high temperatures used, the fusion of ordinary hydrogen (${}^{1}_{1}H$) occurs much too slowly; thus, the heavier isotopes ${}^{2}_{1}H$ (deuterium) and ${}^{3}_{1}H$ (tritium) are employed. The intense heat of the fission explosion starts the fusion of hydrogen nuclei.

$${}^{2}_{1}H + {}^{3}_{1}H \longrightarrow {}^{4}_{2}He + {}^{1}_{0}n$$

The neutron released splits lithium atoms (also incorporated in the bomb), forming more tritium.

$${}^{6}_{3}Li + {}^{1}_{0}n \longrightarrow {}^{4}_{2}He + {}^{3}_{1}H$$

To date, the fusion reactions are useful only for the making of bombs. Research is progressing in the control of nuclear fusion. Controlled fusion would have several advantages over the nuclear fission reactors. The principal fuel, deuterium (${}^{2}_{1}H$), is plentiful and is easily obtained by the fractional electrolysis (the splitting apart by means of electricity) of water, even though only 1 hydrogen atom in 5000 is the deuterium isotope. (We have oceans full of water to work with.) The problem of radioactive wastes would be minimized. The end product, helium, is stable and biologically inert. Escape of tritium might be a problem, because this hydrogen isotope would be readily incorporated into organisms. Tritium (${}^{3}_{1}H$) undergoes beta decay with a half-life of 12.3 years. And there is one other problem associated with any production and use of energy: an unavoidable loss of part of the energy as heat. We would still have to be concerned with thermal pollution.

Great technical difficulties must be overcome before a controlled fusion reaction can be used in the production of energy. Temperatures of 50 000 000 °C must be attained. No material on earth can withstand more than a few thousand degrees. At a temperature of 50 000 000 °C, no molecule can hold together, nor can the atoms from which molecules are made. All atoms are stripped of their electrons. The nuclei and free electrons form a mixture called *plasma* (no relation to blood plasma). There is hope that this plasma can be contained by a strong magnetic field. Scientists in several nations

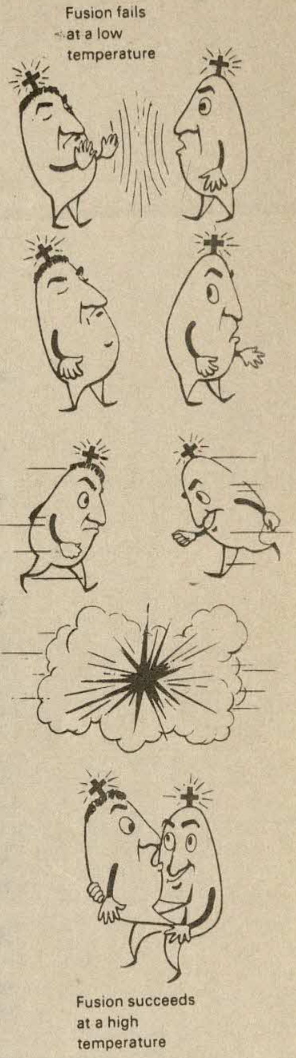

Fusion fails at a low temperature
Fusion succeeds at a high temperature

Figure 3.29 Fusion requires fantastically high temperatures in order to overcome the repulsion between positively charged particles.

are closing in on the conditions necessary for a controlled fusion reaction, but even when that reaction is attained in laboratories, a lot more work will be needed before it becomes a practical source of energy.

3.23 The Nuclear Age Revisited

We live in an age in which fantastic forces have been unleashed. The threat of nuclear war has been a constant specter in our time. Nuclear bombs have been used to destroy cities—and men, women, and children. Science and scientists have been very much involved in it all.

Still, who can believe that the world would be a better place had we not discovered the secrets of the atomic nucleus? For one thing, more lives have been saved through nuclear medicine than have been destroyed by nuclear bombs. And no nuclear bombs have been used in warfare since 1945. Perhaps the terror of nuclear holocaust has done more to prevent World War III than anything else. Nuclear power has not realized the potential once expected. Yet it remains, despite the problems involved, one of our best hopes for a plentiful supply of energy until well into the 21st century.

To maintain the energy output which permits life on earth, the sun, for most of its 4- to 5-billion-year life, has been losing mass at the rate of about 5 000 000 t (5 000 000 000 kg) each second. Lest you worry that this weight loss will shortly remove it (and us) from the universe, let us reassure you. If this loss continued at its present rate, the sun would not disappear until some 20 000 billion years from now. The sun is an immensely massive body.

Problems

1. Define each of the following terms.
   - a. isotope
   - b. deuterium
   - c. alpha particle
   - d. beta particle
   - e. gamma ray
   - f. half-life
   - g. cosmic ray
   - h. positron
   - i. curie (Ci)
   - j. roentgen (R)
   - k. rad
   - l. rem
   - m. Geiger counter
   - n. scintillation counter
   - o. background radiation
   - p. LD_{50}/30 days
   - q. fission
   - r. fusion
   - s. radioisotope
   - t. radioactive tracer
   - u. binding energy
   - v. artificial transmutation
2. How many protons and neutrons are there in each of the following muclei?
   a. $^{206}_{82}Pb$ b. $^{3}_{1}H$ c. $^{60}_{27}Co$ d. $^{233}_{90}Th$.
3. When magnesium-24 (^{24}Mg) is bombarded with neutrons, protons are ejected. What new element is formed? (Hint: Write a balanced nuclear reaction.)
4. A radioactive isotope decays to give an alpha particle and bismuth-211 (^{211}Bi). What was the original element?
5. Lead-209 (^{209}Pb) undergoes beta decay. Write a balanced equation for this reaction.
6. C. E. Bemis and colleagues at Oak Ridge National Laboratory confirmed the identification of element 104, a man-made atom with a half-life of only 4.5 seconds. Only 3000 atoms of the element were created in the tests. How many atoms were left after 4.5 seconds? After 9.0 seconds? After 13.5 seconds?
7. Explain how radioisotopes can be used for therapeutic purposes.
8. Describe one way in which radioisotopes can be used for diagnostic purposes.
9. List two ways in which workers can protect themselves from the radioactive materials they work with.

10. What are some of the characteristics which make technetium-99^{m} such a useful radioisotope for diagnostic purposes?
11. Plutonium is especially hazardous when inhaled or ingested because it emits *alpha* particles ($^{4}_{2}He$). Why would *alpha* particles cause more damage to tissue than *beta* particles ($_{-1}^{0}e$)?
12. Compare nuclear fission and nuclear fusion. Why is energy liberated in both processes?
13. How does a breeder reactor produce more fuel than it consumes?
14. Why are such high temperatures required to cause hydrogen nuclei to fuse?
15. What conditions limit the use of power from nuclear fission?
16. What conditions limit the use of power from nuclear fusion?
17. Discuss the impact of nuclear science on the following. (See the references and readings for resource materials.)
    a. war and peace
    b. industrial progress
    c. medicine
    d. agriculture
    e. our energy needs
    f. human, animal, and plant genetics

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chapter 4

Chemical Bonds

What are chemical bonds that you should be mindful of them? Bonds are the forces that hold atoms and ions together to form molecules and crystals. The type of bonding within molecules also determines the forces between molecules. The state of matter—whether it is solid, liquid, or gas—depends on bonding forces. Bonds even determine the physical shapes of molecules, that is, whether they are spherical or flat, rigid or wobbly.

All this is of great interest to chemists, but what significance can it have for life processes? Let us offer a few pertinent examples.

Carbon has a unique ability to form huge molecules by bonding to itself and to other elements. Those molecules are used to build carbohydrates, fats, proteins, and people.

The bonds of the ozone molecule make life on earth possible. This compound will break apart when struck by sunlight. Its sacrifice stops the sun's ultraviolet rays from burning us all to a crisp.

The bonds of certain chemicals store the energy we need for breathing and for maintaining our heartbeat.

Because carbon monoxide bonds more tightly than oxygen to hemoglobin in our blood, carbon monoxide can kill us.

The action of some drugs depends on the shape (determined by bonding) of the drug molecule. Knowledge of molecular structure has enabled chemists to design not only drugs but also synthetic fabrics, plastics, insecticides, and a thousand other compounds with specific properties.

And if you aren't convinced yet that bonding is important to life, here is one last example. The DNA molecule—the chemical basis of heredity—carries its genetic message in its bonds. Whether an organism is fish, fowl, hippopotamus, or human is determined by the bonding in DNA. The color of your hair and eyes and your general body shape and size were determined by your inheritance of DNA. If you like your appearance, be grateful for chemical bonding. If you're less than thrilled with the color of your hair or the shape of your nose, consider this: our knowledge of chemical bonding may someday permit us to custom-tailor genes, to control to some extent the structure of living matter. That's reason enough to be mindful of chemical bonds.

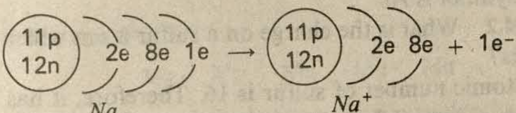
4.1 The Delightful Art of Deduction

In our discussion of the atom and its structure (chapter 2), we followed the historical development of some of the more important concepts. Some of the nuclear concepts (chapter 3) were approached in the same manner. We could continue to look at chemistry in this manner, but that would require several volumes of print—if we got very far—and more of your time, perhaps, than you would care to spend. We won't abandon the historical approach entirely, but we will emphasize that other aspect of scientific enterprise: deduction.

The art of deduction works something like this.

Fact	*Theory*	*Deduction*
The noble gases, such as helium, neon, and argon, are inert (i.e., they undergo few, if any, chemical reactions)	The inertness of the noble gases is due to their electronic structure (each has a filled outermost energy level)	If other elements could alter their electronic structure to become more like noble gases, they would become less reactive

To illustrate, let's look at an atom of the element sodium (Na). It has 11 electrons, 2 in the first energy level, 8 in the second, and 1 in the third. If it could get rid of an electron, it would have the same electronic structure as an atom of the inert gas neon (Ne).



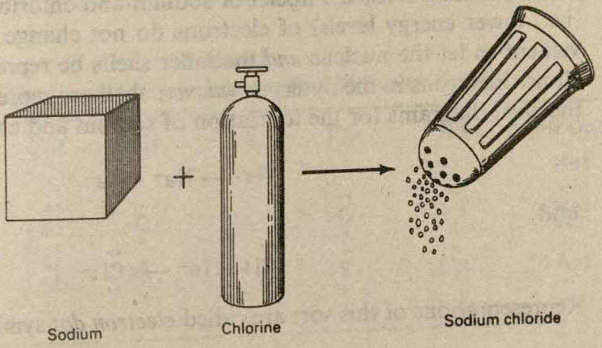
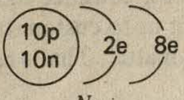


Figure 4.1 Sodium, a soft silvery metal, reacts with chlorine, a greenish gas, to form sodium chloride (ordinary table salt).

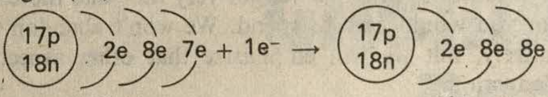
Recall that neon has the structure



Ne

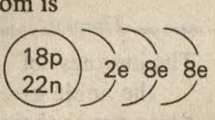
Let us immediately emphasize that the sodium ion (Na^+) and the neon atom (Ne) are not identical. The electron arrangement is the same, but the nuclei—and resulting charges—are not. As long as sodium keeps its 11 protons, it is still a form of sodium. But it is sodium *ion*, not sodium *atom*.

If a chlorine atom (Cl) could gain an electron, it would have the same structure as argon (Ar).



Cl *Cl⁻*

The structure of the argon atom is



Ar

The sodium, having lost an electron, becomes positively charged. It has 11 protons (11+) and only 10 electrons (10−). It is written Na^+ and is called *sodium ion*. The chlorine atom, having gained an electron, becomes negatively charged. It has 17 protons (17+) and 18 electrons (18−). It is written Cl^- and is called *chloride ion*. (More about names later.)

Example 4.1 What is the charge on an aluminum atom which has lost 3 electrons?

The neutral aluminum has 13 electrons and 13 protons (its atomic number is 13). The ion would have 13 protons (13+) and 10 electrons (10−). The net charge on the aluminum ion would be 3+. The symbol is Al^{3+}.

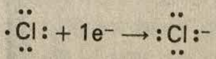
Example 4.2 What is the charge on a sulfur atom which has gained 2 electrons?

The atomic number of sulfur is 16. Therefore, it has 16 protons (16+) and, if it gains 2 electrons, 18 electrons (18−). The net charge is 2−. The symbol is S^{2-}. This is called *sulfide ion*.

In forming ions, the nuclei of sodium and chlorine and the *inner* shells (i.e., lower energy levels) of electrons do not change. Therefore, it is convenient to let the nucleus *and* the inner shells be represented by the *symbol* alone. Electrons in the outer, or *valence*, shell are represented by dots. Thus, the shell diagrams for the ionization of sodium and chlorine are reduced to

$$Na\cdot \longrightarrow Na^+ + 1e^-$$

and

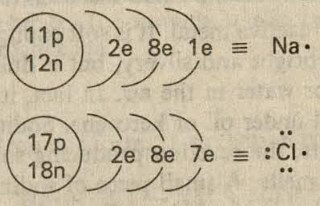


$$\cdot\overset{\cdot\cdot}{\underset{\cdot\cdot}{Cl}}: + 1e^- \longrightarrow :\overset{\cdot\cdot}{\underset{\cdot\cdot}{Cl}}:^-$$

Representations of this sort are called *electron dot* symbols.

4.2 Mystery and Symbolism in Chemistry

The mystery of chemistry to the nonchemist is probably due in large part to chemists' use of symbolism. Chemists find it convenient to represent the sodium atom as Na· rather than as the more complex shell diagram. Therefore, we do just that. And it is easier to write the electron dot symbol for chlorine than the shell diagram. Chemists usually use the shorter form.



It is very easy to write electron dot formulas for elements in the first three periods (horizontal rows) of the periodic chart. The number of electrons in the outer shell is equal to the *group number*. Aluminum (Al) is in Group IIIA; therefore, it has three outer electrons. Sulfur (S) is in Group VIA; thus, it has six outer electrons. This generalization works fairly well for elements in A subgroups even beyond the first three periods. Thus, iodine (I), in Group VIIA, has seven outer electrons. The B subgroups are not quite so regular, and we shall simply ignore them for the moment. **Table 4.1** gives the electron dot formulas for the first 20 elements. Notice that there is a pattern to the way in which the dots are drawn. For elements with four or fewer outer electrons, the electrons are isolated from one another. With the appearance of the fifth electron, a pairing up begins. This is a useful convention—as we shall see shortly.

It doesn't matter whether you draw lithium in any of the following ways. They are all correct.

$$\overset{\cdot}{\text{Li}} \quad \text{Li}\cdot \quad \underset{\cdot}{\text{Li}} \quad \cdot\text{Li}$$

And magnesium can be drawn

$$\overset{\cdot}{\text{Mg}}\cdot \quad \overset{\cdot}{\underset{\cdot}{\text{Mg}}} \quad \cdot\overset{\cdot}{\text{Mg}} \quad \cdot\text{Mg}\cdot \quad \overset{\cdot}{\underset{\cdot}{\text{Mg}}}$$

As long as you show two outer electrons, you're right. As we get into a discussion of compounds, you will see that occasionally sticking to one choice of structures will simplify writing symbols for compounds.

Table 4.1
Electron dot formulas for the first 20 elements

IA	*IIA*	*IIIA*	*IVA*	*VA*	*VIA*	*VIIA*	*Noble Gases*
							He:
H·							
Li·	·Be·	$\cdot\overset{\cdot}{\text{B}}\cdot$	$\cdot\overset{\cdot}{\underset{\cdot}{\text{C}}}\cdot$	$:\overset{\cdot}{\underset{\cdot}{\text{N}}}\cdot$	$:\overset{\cdot\cdot}{\underset{\cdot}{\text{O}}}\cdot$	$:\overset{\cdot\cdot}{\underset{\cdot}{\text{F}}}:$	$:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{Ne}}}:$
Na·	·Mg·	$\cdot\overset{\cdot}{\text{Al}}\cdot$	$\cdot\overset{\cdot}{\underset{\cdot}{\text{Si}}}\cdot$	$:\overset{\cdot}{\underset{\cdot}{\text{P}}}\cdot$	$:\overset{\cdot\cdot}{\underset{\cdot}{\text{S}}}\cdot$	$:\overset{\cdot\cdot}{\underset{\cdot}{\text{Cl}}}:$	$:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{Ar}}}:$
K·	·Ca·						

Symbolism is a convenient, shorthand way of conveying a lot of information in compact form. It is the chemist's most efficient and economical form of communication. Learning this symbolism is much like learning a foreign language. Once you master a certain basic "vocabulary," the rest is easier.

4.3 Sodium Loves Chlorine: The Facts

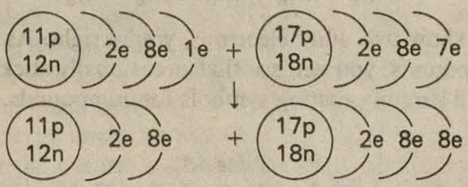
Sodium is a highly reactive metal. It is soft enough to be cut with a knife. When freshly cut it is bright and silvery, but it dulls rapidly as a result of reacting with oxygen or water in the air. In fact, it reacts so readily in air that it is usually stored under oil or kerosene. Sodium reacts violently with water in larger amounts, the reaction producing so much heat energy that any unreacted sodium melts. A small piece of sodium will form a spherical bead after melting and race around on the surface of the water as it continues to react.

Chlorine is a greenish yellow gas. It is familiar as a disinfectant for swimming pools* and city water supplies. (The actual substance added may be a compound which reacts with water to form chlorine.) Who hasn't been swimming in a pool having so much chlorine that it could be tasted? Chlorine is very irritating to the respiratory tract. Indeed, chlorine was used as a poison gas in World War I.

If a piece of sodium is dropped into a flask containing chlorine gas, a violent reaction ensues. A white solid is formed which is very stable. It is a familiar compound—sodium chloride, or table salt.

4.4 The Sodium-Chlorine Reaction: Theory

A sodium atom forms a less reactive species, a sodium ion, by *losing* an electron. A chlorine atom becomes a less reactive chloride ion by *gaining* an electron. A chlorine atom can't just pluck an electron from nowhere, nor can a sodium atom kick out an electron unless something else is willing to take it on. What happens when sodium atoms come into contact with chlorine atoms?** The obvious. A sodium atom transfers an electron to a chlorine atom.



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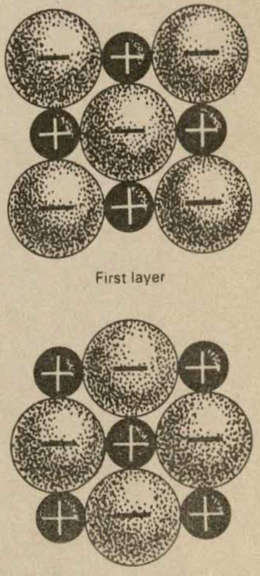
*Bromine, an element in the same family as chlorine, is now used as a disinfectant in some swimming pools.

**Actually, the greenish yellow gas is composed of chlorine *molecules*, each molecule consisting of two atoms. More about that later.

Models Revisited. Scientists sometimes use different models to represent the same system. The model employed in **figure 4.2** is a space-filling model showing the relative sizes of the sodium and chloride ions. Sometimes a ball-and-stick model is employed to better show the geometry of the crystal (**figure 4.3**). From this model it is easy to see the cubic arrangement of the ions. One can also see that for each sodium ion there is one chloride ion; thus, the ratio of ions is one to one, and the simplest formula for the compound is NaCl. The symbols Na and Cl, written together, stand for the compound sodium chloride. The formula is also used to represent one sodium ion and one chloride ion.

Figure 4.2 The arrangement of ions in a sodium chloride crystal.


First layer

Second layer

In the abbreviated electron dot form, this reaction is written

$$\mathrm{Na}\cdot + \cdot\underset{\cdot\cdot}{\ddot{\mathrm{Cl}}}: \longrightarrow \mathrm{Na}^+ + :\underset{\cdot\cdot}{\ddot{\mathrm{Cl}}}:^-$$

The sodium *ion* (Na^+) and the chloride *ion* (Cl^-) not only have electronic structures (sometimes called electron configurations) like those of two noble gases (neon and argon, respectively) but have opposite charges. Everyone knows that opposites attract. And while this rule of thumb may not always work when applied to people, it works quite well for electrically charged particles. Remember that, for even a small amount of salt, there are billions and billions of particles. These arrange themselves in an orderly fashion (**figure 4.2**). These arrangements are repeated in all directions—above and below, left and right, top and bottom—to make up a *crystal* of sodium chloride. Each sodium ion attracts (and is attracted by) six chloride ions (the ones to the front and the back, the top and the bottom, and both sides). Each chloride ion attracts (and is attracted by) the surrounding six sodium ions. The forces holding the crystal together (the attractive forces between positive and negative charges) are called *ionic bonds*.

4.5 More Facts and a Generalization

Potassium (K), a metal similar to sodium, can also react with chlorine to yield a compound called potassium chloride (KCl).

$$\mathrm{K}\cdot + \cdot\underset{\cdot\cdot}{\ddot{\mathrm{Cl}}}: \longrightarrow \mathrm{K}^+ + :\underset{\cdot\cdot}{\ddot{\mathrm{Cl}}}:^-$$

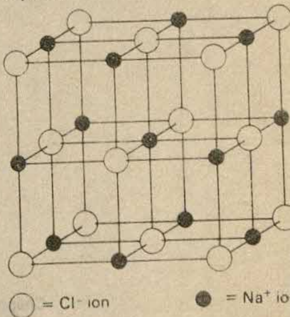
And potassium reacts with bromine, a reddish brown liquid which is chemically similar to chlorine, to form a stable white crystalline solid called potassium bromide (KBr).

$$\mathrm{K}\cdot + \cdot\underset{\cdot\cdot}{\ddot{\mathrm{Br}}}: \longrightarrow \mathrm{K}^+ + :\underset{\cdot\cdot}{\ddot{\mathrm{Br}}}:^-$$

Sodium can also form a compound with bromine: sodium bromide. Magnesium, a metal harder and less reactive than sodium, reacts with oxygen, a colorless gas, to form another stable white crystalline solid called magnesium oxide (MgO).

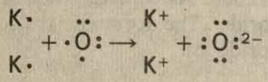
$$\dot{\mathrm{Mg}}\cdot + \cdot\underset{\cdot}{\ddot{\mathrm{O}}}: \longrightarrow \mathrm{Mg}^{2+} + :\underset{\cdot\cdot}{\ddot{\mathrm{O}}}:^{2-}$$

Figure 4.3 Ball-and-stick model of a sodium chloride crystal.



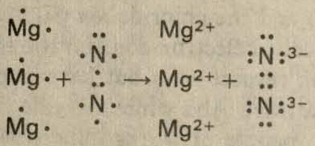
Magnesium must give up two electrons and oxygen must gain two electrons for each to have the same configuration as the noble gas neon.

An atom such as oxygen, which needs two electrons, may react with potassium atoms, which have only one electron to give. In this case, two atoms of potassium are needed for each oxygen atom. The product is potassium oxide (K_2O).



By this process, each potassium atom achieves the argon configuration. Oxygen again assumes the neon configuration.

One last example is the reaction of magnesium and nitrogen to give magnesium nitride (Mg_3N_2).



Each of three magnesium atoms gives up two electrons (a total of six) and each of two nitrogen atoms acquires three (a total of six). Notice that the total positive and negative charges on the products are equal (6+ and 6−).

Generally speaking, those elements on the left side of the periodic chart (especially those on the far left) react with those elements on the far right (excluding the noble gases) to form stable crystalline solids. The theory is that the elements on the left (called *metals*) tend to give up electrons to the elements on the right (*nonmetals*). The crystalline solids are held together by the attraction of oppositely charged ions. This attraction is called an *ionic bond.*

4.6 The Naming Game: Simple Ions and Ionic Compounds

Names of simple positive ions are derived from those of the parent elements by addition of the word *ion*. A sodium atom (Na), upon losing an electron, becomes a *sodium ion* (Na^+). A magnesium atom (Mg), upon losing two electrons, becomes a *magnesium ion* (Mg^{2+}). Names of simple negative ions are derived from those of the parent elements by change of the usual ending to *-ide* and addition of the word *ion*. A chlor*ine* atom (Cl), upon gaining an electron, becomes a chlor*ide ion* (Cl^-). A sulf*ur* atom (S), upon gaining two electrons, becomes a sulf*ide ion* (S^{2-}).

Names and symbols for several important simple ions are given in **table 4.2**. Note that the charge on an ion of a Group IA element is 1+ (usually written simply as +). The charge on an ion of a Group IIA element is 2+, and that on an ion of a Group IIIA element is 3+. You can calculate the charge on the negative ions in the table by subtracting 8 from the group number. For example, the charge on the oxide ion (oxygen is in Group VIA) is $6 - 8 = -2$. The charge on a nitride ion (nitrogen is in Group VA) is $5 - 8 = -3$.

Table 4.2
Symbols and names for some simple ions

Group	*Element*	*Name of Ion*	*Symbol for Ion*
IA	Lithium	Lithium ion	Li^+
	Sodium	Sodium ion	Na^+
	Potassium	Potassium ion	K^+
IIA	Magnesium	Magnesium ion	Mg^{2+}
	Calcium	Calcium ion	Ca^{2+}
IIIA	Aluminum	Aluminum ion	Al^{3+}
VA	Nitrogen	Nitride ion	N^{3-}
VIA	Oxygen	Oxide ion	O^{2-}
	Sulfur	Sulfide ion	S^{2-}
VIIA	Chlorine	Chloride ion	Cl^-
	Bromine	Bromide ion	Br^-
	Iodine	Iodide ion	I^-
IB	Copper	Copper(I) ion (cuprous ion)	Cu^+
		Copper(II) ion (cupric ion)	Cu^{2+}
	Silver	Silver ion	Ag^+
IIB	Zinc	Zinc ion	Zn^{2+}
VIII	Iron	Iron(II) ion (ferrous ion)	Fe^{2+}
		Iron(III) ion (ferric ion)	Fe^{3+}

There is no simple way to determine the most likely charge on ions formed from Group VIII elements and from those in B subgroups. Indeed, you may have noticed that these can form ions with different charges. In such cases, chemists use Roman numerals with the names to indicate the charge. Thus, *iron(II) ion* means Fe^{2+}, and *iron(III) ion* means Fe^{3+}. An older terminology called Fe^{2+} *ferrous ion* and Fe^{3+} *ferric ion*. See similar names for the two copper ions in **table 4.2.**

Compounds such as sodium chloride, potassium bromide, magnesium oxide, and potassium oxide are called *ionic compounds*. The constituent units of these compounds are charged particles—ions. Yet the compound as a whole is electrically neutral. One can use this principle of electrical neutrality to determine the combining ratio of ions. Potassium ions (K^+) would combine with bromide ions (Br^-) in a ratio of one to one. The formula KBr expresses this ratio and represents the compound potassium bromide. The combining ratio (1 : 1) and the ionic charges are understood.

Let's try another example. One calcium ion (Ca^{2+}) combines with *two* chloride ions (Cl^-). This ratio is expressed in the formula $CaCl_2$. In this formula, the ionic charges are understood. As with a coefficient of 1 in algebra, a subscript of 1 is understood where no other number appears, so, in the formula $CaCl_2$, the subscript *1* for calcium ion is understood, but the *2* for chloride is explicitly written (not Ca_1Cl_2 but $CaCl_2$). Thus, $CaCl_2$ not only gives us the combining ratio (1 : 2) but stands for the compound calcium chloride. It is a shorthand way of writing (1 Ca^{2+}) and (2 Cl^-).

You can use the charges on the ions in **table 4.2** to determine formulas for compounds of these elements. You can use a periodic table to predict the charge on ions formed from subgroup A elements, with Group IVA being the dividing line between positive and negative ions.

Example 4.3 What is the formula for sodium sulfide?

First, write the symbols for the ions (positive ion first). Sodium is in Group IA; therefore, its charge is 1+. Sulfur is in Group VIA, and its charge is 2− (6 − 8). The symbols are Na^+ and S^{2-}. The smallest number into which both charges can be evenly divided, that is, the *least common multiple* (LCM), is 2. The least common multiple simply indicates the smallest number of electrons that can be evenly exchanged between the two elements. The subscript for each symbol can be determined by division of its charge (without the plus or minus) into the least common multiple. This step determines how many atoms of each element are needed to supply or accept the smallest common number of electrons. For Na^+,

$$\frac{2\ (\text{LCM})}{1\ (\text{charge})} = 2$$

For S^{2-},

$$\frac{2\ (\text{LCM})}{2\ (\text{charge})} = 1$$

Thus, we have the formula Na_2S_1 (2 Na^+ and 1 S^{2-}), or Na_2S.

Example 4.4 What is the formula for aluminum oxide?

The symbols are Al^{3+} and O^{2-} (Al is in Group IIIA and O is in Group VIA). The LCM is 6. For Al^{3+},

$$\frac{6}{3} = 2$$

For O^{2-},

$$\frac{6}{2} = 3$$

The formula is, therefore, Al_2O_3 (2 Al^{3+} and 3 O^{2-}).

Example 4.5 What is the formula for calcium sulfide?

The symbols are Ca^{2+} and S^{2-}. The LCM is 2. For Ca^{2+},

$$\frac{2}{2} = 1$$

For S^{2-},

$$\frac{2}{2} = 1$$

The formula is, therefore, CaS (Ca^{2+} and S^{2-}).

Naming these ionic compounds is simple. Write the name of the positive ion first and then the name of the negative ion. (The word *ion* is not used. It is understood in each case.)

Example 4.6 What is the name for the compound Na_2S?

Find the constituent ions in **table 4.2.** They are sodium ion (Na^+) and sulfide ion (S^{2-}). The compound is sodium sulfide.

Example 4.7 What is the name for the compound FeS?

There are two kinds of iron ions. Since sulfur exists as the S^{2-} ion and one iron ion is combined with it, the iron ion in this compound must be Fe^{2+}. The name of FeS is iron(II) sulfide.

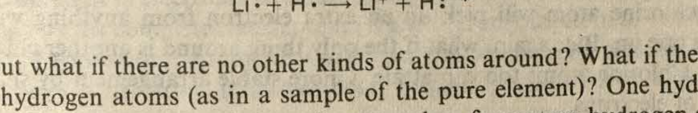
Example 4.8 What is the name of the compound $FeCl_3$?

Since the charge on the chloride ion is 1 – and three of these ions are combined with one iron ion, the iron ion must be Fe^{3+}. The name of $FeCl_3$ is iron(III) chloride.

Ionic compounds generally exist as crystalline solids. However, many of them are soluble in water. Ionic compounds are found dissolved in all natural waters—including the water in the cells of our bodies—where they are involved in such critical functions as the transmission of nerve impulses.

4.7 Covalent Bonds: A Share-the-Wealth Plan for Electron-deficient Atoms

One might expect a hydrogen atom, with its one electron, to tend to acquire an electron and assume the helium structure. Indeed, hydrogen atoms do just that in the presence of atoms of a reactive metal such as lithium, that is, a metal that is eager to give up an electron.



Using electron dot symbols, we would write

$$\mathrm{Li\cdot + H\cdot \longrightarrow Li^+ + H{:}^-}*$$

But what if there are no other kinds of atoms around? What if there are only hydrogen atoms (as in a sample of the pure element)? One hydrogen atom can hardly grab an electron from another, for among hydrogen atoms all have an equal attraction for electrons. (Even more important, perhaps,

---

*$H{:}^-$ is a hydride ion. The compound formed, often simply represented by the formula LiH, is lithium hydride. This compound is sometimes used to "store" hydrogen in the solid state. It reacts readily with water to form hydrogen gas.

$$\mathrm{LiH + H_2O \longrightarrow LiOH + H_2}$$

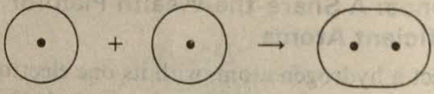
Only 8 g (slightly over $\frac{1}{4}$ oz) will produce over 20 ℓ of hydrogen gas at ordinary temperatures and pressures.

We cannot emphasize too strongly the difference between ions and the atoms from which they are made. They are as different as a whole peach (an atom) and a peach pit (an ion). The names and symbols may look a lot alike, but the substances themselves are quite different. Unfortunately, the situation is confused because people talk about needing "iron" to perk up "tired blood" and "calcium" for healthy teeth and bones. What they really mean is iron(II) *ions* (Fe^{2+}) and calcium ions (Ca^{2+}). No one would think of eating iron nails to get "iron." Nor would they eat highly reactive calcium metal. Although careful distinction is not always made by laypersons, we will try to use precise terminology here.

hydrogen atoms do not have a tendency to lose electrons at all, for the result would be a highly reactive bare proton—the hydrogen nucleus.) Hydrogen atoms can compromise, however, by *sharing* a pair of electrons.

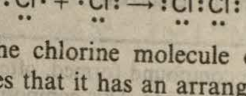
$$\mathrm{H}\cdot + \cdot\mathrm{H} \longrightarrow \mathrm{H}:\mathrm{H}$$

It is as if the two hydrogen atoms, in approaching one another, get their electron clouds or orbitals so thoroughly enmeshed that they can't easily pull them apart again.



Most of the time the electrons are located between the two nuclei. The electron dot representation usually used, H:H, is therefore a fairly good picture. If we were to attribute human qualities to hydrogen atoms, we would suggest that they are a bit thick, a little slow on the uptake. Each one looks around, sees two electrons, and happily decides that they are its very own electrons and that, therefore, it has an arrangement like that of helium, one of the noble gases. This combination of hydrogen atoms is called a *hydrogen molecule*. The bond formed by a shared pair of electrons is called a *covalent bond*.

A chlorine atom will pick up an extra electron from anything willing to give one up. But, again, what if the only thing around is another chlorine atom? Chlorine atoms too can attain a more stable arrangement by sharing a pair of electrons.



$$:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}\cdot + \cdot\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}: \longrightarrow :\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:$$

Each chlorine atom in the chlorine molecule can count eight electrons around itself and concludes that it has an arrangement like that of a noble gas, argon in this instance. This stable "octet" of electrons is the arrangement characteristic of the noble gases, except helium. Covalently bonded atoms that we shall consider, except hydrogen, follow the "octet" rule; that is, they seek an arrangement which will surround them with eight electrons. The shared pair of electrons in the chlorine molecule also creates a covalent bond.

For simplicity, the hydrogen molecule is often represented as H_2 and the chlorine molecule as Cl_2. The subscripts indicate two atoms *per mole-*

cule. In each case, the covalent bond between the atoms is understood. Sometimes the covalent bond is indicated by a dash, H—H and Cl—Cl.

This sharing of electrons is not limited to one pair of electrons. Consider, for example, the nitrogen atom. Its electron dot symbol is

$$\cdot\overset{\cdot}{\underset{\cdot}{\mathrm{N}}}:$$

Now we know this little devil can't be happy after all we've learned about the octet rule. It has only five electrons in its outermost shell. It could share a pair of electrons with another nitrogen atom and would then look like this:

$$:\overset{\cdot}{\underset{\cdot}{\mathrm{N}}}:\overset{\cdot}{\underset{\cdot}{\mathrm{N}}}:$$

But while atoms may be a bit slow on the uptake, they are not stupid. Each one can see that in this arrangement, only six electrons surround it. And six is not eight. Each sees that it has two electrons hanging out there without partners, so, to solve the dilemma, each nitrogen agrees to share two additional pairs of electrons, for a total of three pairs.

$$:\mathrm{N}:::\mathrm{N}:\ (\text{or } :\mathrm{N}\,\vdots\vdots\,\mathrm{N}: \text{ or } \mathrm{N}\equiv\mathrm{N})$$

In drawing the nitrogen molecule (N_2), we have simply drawn all the electrons that are being shared in the space between the two atoms. Each nitrogen has now satisfied the octet rule. A compound in which three pairs of electrons (a total of six individual electrons) are being shared is said to contain a *triple* bond. Note that we could have drawn the *unshared* pair of electrons above or below the atomic symbol. Such a drawing would represent the same compound.

4.8 Some Atoms Are More Equal Than Others: Polar Covalent Bonds

So far we have seen that atoms combine in two different ways. Some that are quite different in electronic structure (from opposite ends of the periodic table) react by the complete transfer of an electron from one atom to another (ionic bond formation). Atoms that are identical combine by sharing one or more pairs of electrons (covalent bond formation). Now, let's look at some "in-betweeners."

Hydrogen and chlorine react to form a colorless gas called hydrogen chloride. This reaction may be represented schematically by

$$\mathrm{H}\cdot + \cdot\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}: \longrightarrow \mathrm{H}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:\ (\text{or } \mathrm{H{-}Cl})$$

Both hydrogen and chlorine want an electron, so they compromise by sharing and forming a covalent bond. Since both hydrogen and chlorine actually consist of diatomic molecules, the reaction is more accurately represented by the scheme

$$\mathrm{H}:\mathrm{H} + :\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}: \longrightarrow 2\ \mathrm{H}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:$$

One might reasonably ask why the hydrogen molecule and the chlorine molecule react at all. Have we not just explained that they themselves were formed to provide a more stable arrangement of electrons? Yes, indeed, we did say that. But there is stable and there is more stable. The chlorine molecule represents a more stable arrangement than two separate chlorine atoms. But, given the opportunity, a chlorine atom would rather form a bond with a hydrogen atom than with another chlorine atom. Why? Tune in again (in chapter 5) for the answer.

Figure 4.4 Chlorine hogs the electron blanket, leaving hydrogen partially, but positively, exposed. To hydrogen's pleas for more cover, chlorine's answer is partially negative.

For the sake of convenience and simplicity, the reaction of hydrogen (molecule) and chlorine (molecule) to form hydrogen chloride can be reduced to

$$H_2 + Cl_2 \rightarrow 2\,HCl$$

Molecules of hydrogen chloride consist of one atom of hydrogen and one atom of chlorine. These unlike atoms share a pair of electrons. Sharing does not mean sharing equally, though. A wealth of evidence points to the fact that chlorine atoms have a greater attraction for a shared pair of electrons than do hydrogen atoms. Chlorine is said to be more *electronegative* than hydrogen. Thus, shared electrons spend more time near the chlorine atom than they do near the hydrogen atom. If you think of an orbital as a fuzzy-looking cloud, then the cloud is denser near the chlorine. Since the electrons are more often found in the vicinity of the chlorine nucleus, that end of the molecule is more negative than the other. The hydrogen end is slightly positive. Such a covalent bond, in which the electron sharing is not equal, is called a *polar covalent bond*, or simply a *polar bond*. Covalent bonds in which electrons are equally shared (as in Cl_2 or H_2) are referred to as *nonpolar covalent bonds* to distinguish them from polar bonds. The polar covalent bond is *not* an ionic bond. In the latter, one atom completely loses an electron. In the former, the atom at the positive end of the bond (hydrogen in HCl) still has some share in the bonding pair of electrons. To distinguish this arrangement from that in an ionic bond, the following notation is used.

$$\overset{\delta+}{H}\text{—}\overset{\delta-}{Cl}$$

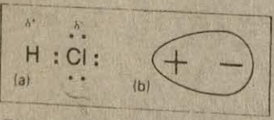


Figure 4.5 Representation of the polar hydrogen chloride molecule. (a) The electron dot formula, with the shared electron pair shown nearer chlorine. The symbols δ^+ and δ^- indicate partial positive and negative charges, respectively. (b) A diagram showing the hydrogen chloride molecule.

The line between the two atoms represents the covalent bond, a pair of shared electrons. The $\delta+$ and $\delta-$ (read "delta plus" and "delta minus") signify which end is partially positive and which is partially negative (the word *partially* is used to distinguish this charge from the full charge an ion has). This unequal sharing of electrons has a marked effect on the properties of a compound.

The gas hydrogen chloride dissolves readily in water. The aqueous solution formed is called hydrochloric acid (sometimes muriatic acid). This acid is used for, among other things, cleaning toilet bowls and removing excess mortar from new brick buildings. Hydrochloric acid is also the well-known "stomach acid." Acids will be defined and further discussed in chapter 10.

4.9 Electronegativity

Before we look at the structure of any more molecules, we should consider in more detail the concept of electronegativity. When one speaks of the electronegativity of an atom, one is describing its tendency to attract electrons to itself. The atoms to the right in the periodic table are, in general, more electronegative than those to the left. The ones on the right are precisely those atoms which, in forming ions, tend to gain electrons and form negative ions. The ones on the left, the metals, tend to give up electrons, to become positive ions. The more electronegative an atom, the greater its tendency to pull the electrons in the bond toward its end of the bond when it is involved in covalent bonds.

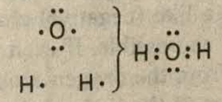
The most electronegative element in the periodic table is fluorine, in the upper right-hand corner of the table. You can use this fact as a guide. Within a period (a row) of the table, elements become more electronegative toward the right. Oxygen is more electronegative than nitrogen. Within a group (column) of the table, elements become less electronegative toward the bottom. Chlorine is less electronegative than fluorine. The comparison is not quite so straightforward when one is considering two elements which are in neither the same period nor the same group.

Hydrogen is difficult to place (see the unique position assigned to it in the periodic table, on the inside front cover). It could be placed in Group IA, because, like lithium, it has one electron in its outer shell, but it really isn't much like the Group IA metals. Or it could be placed in Group VIIA, because, like fluorine, it is just one electron short of looking like a noble gas. However, hydrogen isn't nearly as electronegative as fluorine. If you look at a number of versions of the periodic table, you'll see that chemists still haven't decided what to do with it. In this book, we have taken the coward's way out. We've placed it at the top middle, away from everything. Its electronegativity fits that position. It will take electrons from an atom that really wants to get rid of them (lithium, for example), and it will shift electrons to an electronegative element (fluorine, for example).

To consider covalent bonding in any detail, you must have an understanding of this concept of electronegativity.

4.10 Water: A Crooked Molecule

Water is one of the most familiar chemical substances. The electrolysis experiment of Nicholson and Carlisle (chapter 2) and ample evidence since their time indicate that the molecular formula for water is H_2O. When we considered oxygen previously, we noted that it wanted to share two pairs of electrons, so that it could be surrounded by a total of eight. But a hydrogen atom only wants to share one pair of electrons. Therefore, an oxygen atom must bond with two hydrogen atoms.



This arrangement completes the valence shell of oxygen, which now has the neon structure. It also completes the outer shell of the hydrogen atoms, each of which now has the helium structure.

This two-dimensional representation for the water molecule adequately

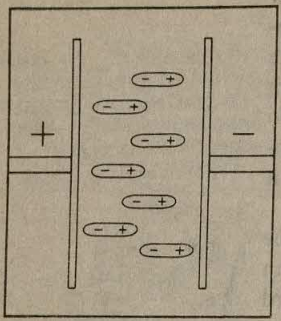
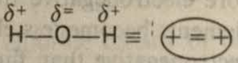


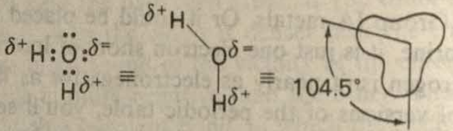
Figure 4.6 Molecules aligned as dipoles between charged plates.

explains many of the properties of water, but there are other phenomena that can be explained only by a more detailed picture. For example, when placed between two charged plates, water molecules align themselves as dipoles (**figure 4.6**). By a *dipole* we mean a molecule which has a positive end and a negative end.

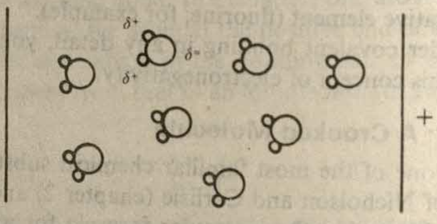
It is evident that hydrogen-oxygen bonds ought to be polar, for hydrogen and oxygen would not be expected to share a pair of electrons equally. Oxygen is a strongly electronegative atom. However, if the atoms were in a straight row (that is, in a linear arrangement), the two polar bonds would cancel one another and there would be no net dipole.



To act like dipoles, the atoms must be arranged on an angle. Precise (but indirect) measurements with sophisticated instruments show that the bond angle (that is, the angle between the two bonds) is 104.5°. Thus, the charge distribution is as follows.

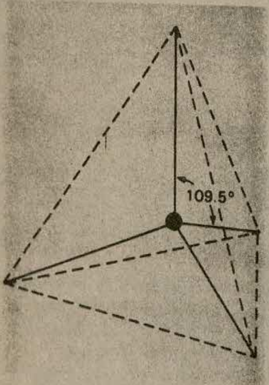


The molecules would align themselves between charged plates in the following way.



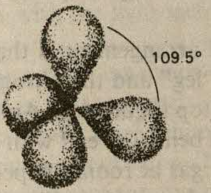
There are several theories of chemical bonding that account for the shape of the water molecule. One of the simplest and most satisfying is the valence shell electron pair repulsion (VSEPR) theory. According to this theory, the arrangement of the bonds in water can be explained as follows. There are four pairs of electrons surrounding the oxygen atom in the water molecule. Since all electrons bear a like (negative) charge, it is reasonable to expect them to get as far apart as possible. If each pair of electrons is represented as a line extending out from the oxygen atom, the farthest apart these lines can get is 109.5°. Further, if the ends of these lines were all connected, the connecting line would inscribe a regular tetrahedron (**figure 4.7**).

Figure 4.7 The four electron pairs around a central atom point toward the corners of a regular tetrahedron. Each angle is 109.5°.

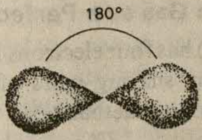


The predicted tetrahedral angle of 109.5° is not far from the actual value of 104.5° for water. The disagreement is accounted for by the theory that in water the *nonbonding pairs* of electrons, those that are not shared with hydrogen atoms, occupy a greater volume than the bonding pairs because the

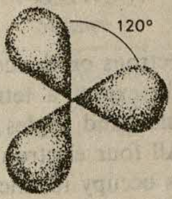
The tetrahedral arrangement is not limited to molecules. The farthest apart any four equivalent things can get, if they are tied to a common center, is 109.5°. Four balloons tied together would automatically take up the tetrahedral shape.



Two balloons so tied, as you might expect, would point in opposite directions. To put it more elegantly, they would take up positions such that the angle between them would be 180°.



Three balloons would all lie in the same plane and assume positions such that the angles between them would be 120°.

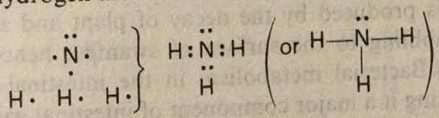


nonbonding pairs are not squeezed between *two* nuclei. Thus, the nonbonding pairs push the bonding pairs a little bit closer together.

We will take a further look at the unique properties of water in chapter 7.

4.11 Ammonia: An Unshared Pair on a Tripod

An atom of the element nitrogen (N) has five electrons in its valence shell. It can assume the neon configuration by sharing three pairs of electrons with *three* hydrogen atoms and forming the compound ammonia.



$$\left.\begin{matrix}\cdot\ddot{\text{N}}\cdot \\ \cdot \\ \text{H}\cdot\ \ \text{H}\cdot\ \ \text{H}\cdot\end{matrix}\right\}\ \ \text{H}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\text{N}}}:\text{H}\ \ \left(\text{or}\ \ \text{H—}\overset{\cdot\cdot}{\text{N}}\text{—H}\right)$$

There are four pairs of electrons on the central nitrogen atom in the ammonia molecule. Using the electron pair repulsion theory, one would expect a tetrahedral arrangement of the four pairs and bond angles of 109.5°. The actual

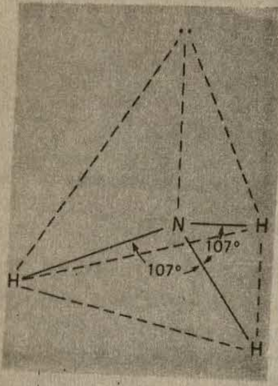


Figure 4.8 The pyramidal ammonia molecule.

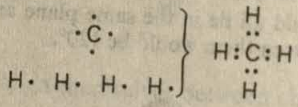
bond angles are 107°, quite close to the theoretical value. Presumably the unshared pair occupies a greater volume than the shared pairs occupy, pushing the latter slightly closer together. The bond angles in ammonia are larger (closer to 109.5°) than the bond angle in water because there is only one unshared pair of electrons doing the pushing in ammonia while there are two in water.

In ammonia, the bond arrangement is that of a tripod with a hydrogen atom at the end of each "leg" and the nitrogen atom with its unshared pair of electrons sitting at the top (**figure 4.8**). Ammonia is also a polar molecule, with the top of the tripod being the end with the partial negative charge.

Ammonia (NH_3) is a gas at room temperature. Vast quantities of it are compressed into tanks and used as fertilizer. Ammonia is quite soluble in water. It forms an aqueous solution which is basic, that is, one which will neutralize acids (chapter 10). Such aqueous preparations are familiar household cleansing solutions.

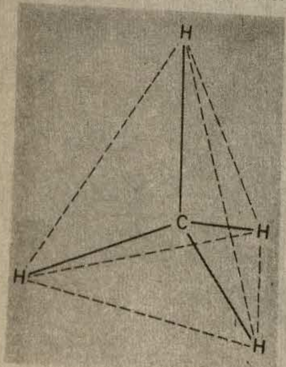
4.12 Methane: Marsh Gas as a Perfect Tetrahedron

An atom of carbon (C) has four electrons in its valence shell. It can assume the neon configuration by sharing pairs of electrons with four hydrogen atoms, forming the compound methane.



$$\left.\begin{array}{c}\cdot\dot{\underset{\cdot}{\mathrm{C}}}\cdot\\ \mathrm{H}\cdot\ \ \mathrm{H}\cdot\ \ \mathrm{H}\cdot\ \ \mathrm{H}\cdot\end{array}\right\}\ \begin{array}{c}\mathrm{H}\\ \mathrm{H}:\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{C}}}:\mathrm{H}\\ \mathrm{H}\end{array}$$

Figure 4.9 The tetrahedral methane molecule.



There are four pairs of electrons on the central carbon in methane. By the VSEPR theory, one would expect a tetrahedral arrangement and bond angles of 109.5°. The actual bond angles are 109.5°, in perfect agreement with theory (**figure 4.9**). All four electron pairs are shared with hydrogen atoms; thus, all four pairs occupy identical volumes. The arrangement of the four bonds would make methane a nonpolar molecule; any polarity in the individual bonds would mutually cancel out. The situation here is analogous to that pointed out for a "straight" arrangement of the water molecule (p. 94). In fact, carbon and hydrogen have very similar electronegativities, so the individual bonds themselves would not be expected to be very polar.

Methane is represented by the formula CH_4. It is the principal component of natural gas, used as a fuel in many parts of the country. Methane burns with a hot flame, and if sufficient oxygen is present, the only products are the relatively innocuous carbon dioxide and water.

Methane is produced by the decay of plant and animal material. It is often seen bubbling to the surface of swamps; hence its common name "marsh gas." Bacterial metabolism in the intestinal tract also produces methane, making it a major component of intestinal gas.

4.13 Some Rules for the Molecular Architect

We have seen in the preceding section how different atoms form different numbers of bonds. Hydrogen forms one bond, chlorine one, oxygen two, nitrogen three, and carbon four. The number of covalent bonds that an atom can form is called its *valence*. Recall that the lowest energy level of an atom can be occupied by at most two electrons. These may be either shared or unshared. The hydrogen atom has one electron. It can form *one* bond by sharing this electron with another atom. The other atom also furnishes one electron to form a shared pair with the hydrogen electron. Hydrogen is said to be *univalent*.

The helium (He) atom has a filled innermost shell. It cannot share electrons with other atoms; hence its valence is zero.

The second energy level can hold a maximum of eight electrons (that is, four pairs of electrons). In the element neon (Ne), this shell is filled, and neon forms no bonds. Its valence is zero (or, one could say, it has *no* valence).

The fluorine atom has seven electrons in its outer, or valence, shell. It can therefore form one bond by sharing one electron with another element. The other element furnishes one electron to form a shared pair. Thus, fluorine, like hydrogen, is univalent, having three unshared pairs of electrons and the capacity to form one bond involving one shared pair.

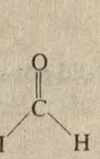
Similar considerations reveal that oxygen is *bivalent*, nitrogen is *trivalent*, and carbon is *tetravalent*. These guidelines for the molecular architect are summarized and illustrated in **table 4.3.**

You will notice that the table does not include all of the elements in which the second energy level is not yet filled. (Lithium is one that's missing.) That's because these elements have a tendency to form ionic bonds rather

I BEG YOUR PARDON!
WELL.... REALLY!

Figure 4.10 Methane is formed in the intestinal tract by bacterial action.

Table 4.3
Valence

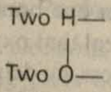
Electron Dot Picture	*Valence Bond Picture*	*Number of Bonds (Valence)*	*Representative Molecules*
H·	H—	1	H—H H—Cl
He:	—	0	
$\cdot\overset{\cdot}{\underset{\cdot}{\mathrm{C}}}\cdot$	$-\overset{\vert}{\underset{\vert}{\mathrm{C}}}-$	4	$\mathrm{H-\overset{\overset{H}{\vert}}{\underset{\underset{H}{\vert}}{C}}-H}$ $\begin{matrix}\mathrm{O}\\ \Vert\\ \mathrm{C}\\ \Vert\\ \mathrm{O}\end{matrix}$
$\cdot\overset{\cdot\cdot}{\underset{\cdot}{\mathrm{N}}}\cdot$	$-\overset{\cdot\cdot}{\underset{\vert}{\mathrm{N}}}-$	3	$\mathrm{H-\overset{\cdot\cdot}{\underset{\underset{H}{\vert}}{N}}-H}$ $:\mathrm{N\equiv N}:$
$\cdot\overset{\cdot\cdot}{\underset{\cdot}{\mathrm{O}}}:$	$-\overset{\cdot\cdot}{\underset{\vert}{\mathrm{O}}}:$	2	$\mathrm{H-\overset{\cdot\cdot}{\underset{\underset{H}{\vert}}{O}}}:$ 
$\cdot\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{F}}}:$	$-\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{F}}}:$	1	H—F F—F
$\cdot\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:$	$-\overset{\cdot\cdot}{\underset{\cdot\cdot}{\mathrm{Cl}}}:$	1	H—Cl Cl—Cl

than the covalent bonds in which we are presently interested. The electron dot formulas of beryllium and boron are

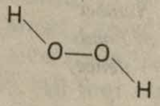
·Be·   ·Ḃ·

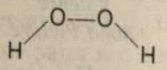
These two elements can use their unshared electrons to form two and three covalent bonds, respectively. When they do so, however, they do not achieve a noble gas configuration. Therefore, the compounds thus formed are ordinarily quite reactive.

There is a chemical substance called hydrogen peroxide. Chemical analysis shows that each molecule of hydrogen peroxide is composed of two hydrogen atoms and two oxygen atoms. This information is indicated in the formula H_2O_2. What is the structure of the hydrogen peroxide molecule? The parts list is as follows.

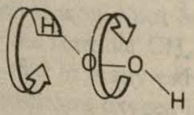


For the sake of conserving ink, we will omit drawing the nonbonding electrons, that is, the unshared pairs. No connections can be made *through* hydrogen, for each hydrogen has only one connector. To be in between you have to be able to hold on with two hands (or bonds) at least. The only kind of molecule that one can make using two atoms of hydrogen and two of oxygen is shown below in I.


I


II

Arrangement II, which may look like a different molecule, really isn't. Arrangement I can be converted into arrangement II—and vice versa—by rotation (spinning) about the O—O bond.

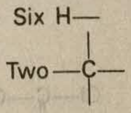


We did not offer

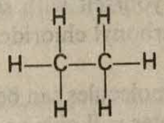
H—O—O—H

as a possibility. The molecule is really bent (for precisely the same reason that the water molecule is bent). We did not draw in the unshared electron pairs, but they're still there, taking up space. You might see the structure drawn in this straight form, but that is because it is easier to type the straight formula. And this formula does show which atoms are attached to which. However, the presumption is that we all understand the molecule is really bent.

Let's build another molecule. There is a chemical substance called ethane which, like methane, is a constituent of natural gas. Chemical analysis indicates that the molecular formula for ethane is C_2H_6. By the rules of molecular architecture, the molecule can be put together as follows. The parts list includes



The only way six atoms of hydrogen and two of carbon can be put together according to the rules is



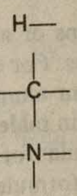
The molecule is really three-dimensional (carbon's bonds are arranged in the tetrahedral form). The restrictions imposed by the two-dimensional nature of the printed page have caused us to draw it flat here.

Methane (CH_4) and ethane (C_2H_6) are merely the first members of a series of similar compounds called *alkanes* or *saturated hydrocarbons*. Other members of the series will be discussed in chapter 14.

Following are a few other examples of molecule building.

Example 4.9 If the *molecular formula* of a substance is HCN, what is its *structural formula* (the formula which shows the attachment of the atoms)?

We have



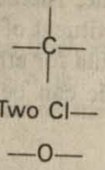
The carbon needs to form four bonds, the hydrogen needs to form one bond, and the nitrogen needs to form three bonds. The only way this combination can be put together is

$$H{-}C{\equiv}N$$

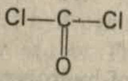
Note that the carbon has formed four bonds (a single and a triple), the nitrogen has formed three, and the hydrogen has formed one.

Example 4.10 If the molecular formula of a substance is $COCl_2$, what is its structural formula?

The parts are



The formula is

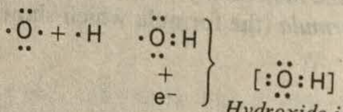


If you attempt to attach the chlorine atoms to the oxygen rather than the carbon, you'll find yourself with some leftover connectors. Try it. (The compound is carbonyl chloride, alias phosgene, a poisonous gas.)

Extremely complicated molecules can be constructed by these rules. Problem 9 at the end of the chapter will give you some practice in drawing a few simpler ones.

4.15 Hanging In There Together: Complex Ions

There are many familiar substances (for example, sodium hydroxide, also called *lye*) that have both ionic and covalent bonds. As might be expected, sodium hydroxide contains sodium ions (Na^+). The "hydroxide" part contains an oxygen atom covalently bonded to hydrogen. There is an "extra" electron in this unit which gives it a negative charge.



There are many such groups of atoms in nature. They hang together through most chemical reactions. For example, sodium hydroxide will react with aluminum chloride to form aluminum hydroxide. A list of the more common complex ions is given in **table 4.4**, which you can use, in combination with **table 4.2**, to write formulas for compounds containing complex ions.

Example 4.11 What is the formula for sodium sulfate?

First, write the formulas for the ions.

$$Na^+ \quad SO_4^{2-}$$

The least common multiple is 2. The formula is therefore Na_2SO_4.

Example 4.12 What is the formula for ammonium sulfide?

The ions are

$$NH_4^+ \quad S^{2-}$$

Table 4.4
Some common complex ions

Charge	*Name*	*Formula*
1+	Ammonium ion	NH_4^+
1−	Hydrogen carbonate (bicarbonate) ion	HCO_3^-
	Hydrogen sulfate (bisulfate) ion	HSO_4^-
	Acetate ion	$CH_3CO_2^-$ (or $C_2H_3O_2^-$)
	Nitrite ion	NO_2^-
	Nitrate ion	NO_3^-
	Cyanide ion	CN^-
	Hydroxide ion	OH^-
	Dihydrogen phosphate ion	$H_2PO_4^-$
2−	Carbonate ion	CO_3^{2-}
	Sulfate ion	SO_4^{2-}
	Monohydrogen phosphate ion	HPO_4^{2-}
	Oxalate ion	$C_2O_4^{2-}$
3−	Phosphate ion	PO_4^{3-}

The least common multiple is 2. The formula is $(NH_4)_2S$. The parentheses are necessary to indicate that the entire ammonium unit is taken twice.

Example 4.13 What is the formula for ammonium nitrate?

The ions are

$$NH_4^+ \quad NO_3^-$$

The least common multiple is 1. The formula for ammonium nitrate is NH_4NO_3.

Example 4.14 What is the name for the compound NaCN?

The ions are

$$Na^+ \quad CN^-$$

The name is sodium cyanide.

Example 4.15 What is the name for KH_2PO_4?

The ions are

$$K^+ \quad H_2PO_4^-$$

The name is potassium dihydrogen phosphate.

Example 4.16 What is the name for $(NH_4)_2HPO_4$?

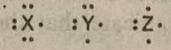
The ions are

$$NH_4^+ \quad HPO_4^{2-}$$

The name is ammonium monohydrogen phosphate.

Problems

1. What is the theoretical difference between a sodium atom and a sodium ion? How do sodium atoms differ from sodium ions in terms of properties?
2. What is the theoretical difference between a chlorine atom, a chlorine molecule, and a chloride ion? How do they differ in properties?
3. What is wrong with the expression "a molecule of sodium chloride"?
4. Write correct formulas for each of the following compounds.
   a. lithium fluoride
   b. calcium iodide
   c. aluminum bromide
   d. magnesium sulfate
   e. ammonium phosphate
   f. sodium oxalate
   g. calcium monohydrogen phosphate
   h. magnesium phosphate
   i. potassium nitrate
   j. iron(III) hydroxide
   k. aluminum sulfide
   l. copper(II) cyanide
5. Give the correct name for the compound represented by each of these formulas.
   a. NaBr
   b. $CaCl_2$
   c. Al_2O_3
   d. $CaSO_4$
   e. $NaHSO_4$
   f. $KHCO_3$
   g. $Mg(CH_3CO_2)_2$
   h. $Al(C_2H_3O_2)_3$
   i. $(NH_4)_3PO_4$
   j. $(NH_4)_2C_2O_4$
   k. KNO_2
   l. Na_2HPO_4
   m. KCN
   n. $Al(OH)_3$
   o. $Ca(H_2PO_4)_2$
   p. Na_2CO_3
   q. $Mg(HCO_3)_2$
   r. NH_4I
   s. $Ca(HSO_4)_2$
   t. $NaNO_3$
6. Give examples of univalent, bivalent, trivalent, and tetravalent elements.
7. Use the VSEPR theory to predict the shape for these molecules.
   a. hydrogen sulfide (H_2S)
   b. silane (SiH_4)
   c. beryllium chloride ($BeCl_2$)
   d. boron fluoride (BF_3)
8. Consider the hypothetical elements X, Y, and Z with electron dot symbols



$$:\overset{\cdot\cdot}{\underset{\cdot\cdot}{X}}\cdot \qquad :\overset{\cdot\cdot}{\underset{\cdot}{Y}}\cdot \qquad :\overset{\cdot}{\underset{\cdot}{Z}}\cdot$$

   a. To which group in the periodic table would each belong?
   b. Write the electron dot formula for the simplest compound of each with hydrogen.
   c. What would be the shape of each of these compounds?
   d. Write electron dot formulas for the ions formed when X and Y react with sodium.
9. Use the valence rules to construct structural formulas for the following.
   a. CH_4O
   b. CH_5N
   c. NOH_3
   d. N_2H_4
   e. NF_3
   f. C_2H_4
   g. C_2H_2

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chapter 5

Energy and Equilibria

The complex chemical processes in the living cell involve changes in energy as well as changes in chemical composition. Some reactions provide the energy that keeps the cell alive and well. Other reactions, vital to life processes, require an input of energy.

Chemical reactions proceed at various rates. Some are explosively fast; others, exceedingly slow. Rates are affected by a number of factors. Perhaps the most important of these factors, for living organisms, are complex molecules called enzymes which accelerate reaction rates enormously. Yet, strange as it may seem, the enzymes are still there unchanged *after* doing their job.

Chemical reactions also proceed to different extents. In some, the reactants are converted entirely to products; these reactions are said to go to *completion.* In others, the products react, re-forming the original starting materials. These reactions, outside the cell, come to equilibrium. In a living cell, equilibrium would be deadly. The cellular processes must go to completion—or very nearly so. Products can become reactants in the body, but not under equilibrium conditions.

In this chapter we will examine energy changes, reaction rates, and equilibria. For the most part, we will deal with simple, nonliving systems. The principles developed, however, will be exceedingly important in later chapters, where we will deal with the more complex chemistry of living cells.

5.1 Chemistry: Where the Reactions Are

Chemistry is a study of matter and the changes it undergoes. More than that, it is a study of the energy that brings about those changes—or the energy that is released when those changes occur. In chapter 4, we discussed the symbols and formulas that have been invented to represent elements and compounds. Now let's look at a shorthand way of describing chemical changes—the *chemical equation.*

Carbon reacts with oxygen to form carbon dioxide. In the chemical shorthand this reaction is written

$$C + O_2 \longrightarrow CO_2$$

The plus sign (+) indicates addition of carbon to oxygen (or vice versa) or a mixing of the two in some manner. The arrow (→) is often read "yields." Substances on the left of the arrow are *reactants* or *starting materials*. Those on the right are the *products* of the reaction. The conventions here are like those we used in writing nuclear equations (chapter 3). Now, however, the nucleus will remain untouched. The chemical reactions we are going to look at will involve only electronic structures.

Chemical equations have meaning on the atomic and molecular level. The equation

$$C + O_2 \longrightarrow CO_2$$

means that one atom of carbon (C) reacts with one molecule of oxygen (O_2) to produce one molecule of carbon dioxide (CO_2).

Not all chemical reactions are so simply represented. Hydrogen reacts with oxygen to form water. We can write this reaction as

$$H_2 + O_2 \longrightarrow H_2O$$

This representation, however, is not consistent with the law of conservation of matter. There are two oxygen atoms shown among the reactants (as O_2) and only one among the products (in H_2O). For the equation to represent correctly the chemical happening, it must be *balanced*. To balance the oxygen atoms we need only place the coefficient *2* in front of the formula for water.

$$H_2 + O_2 \longrightarrow 2\ H_2O$$

This coefficient means that there are *two* molecules of water involved. As is the case with subscripts (chapter 4), a coefficient of 1 is understood where no other number appears. A coefficient preceding a formula multiplies everything in the formula. In the second equation, the coefficient *2* not only increases the number of oxygen atoms to two, but also increases the number of hydrogen atoms to four.

But that equation is still not balanced. We took care of oxygen at the expense of messing up hydrogen. To balance hydrogen, we place a coefficient *2* in front of the H_2.

$$2\ H_2 + O_2 \longrightarrow 2\ H_2O$$

Now there are enough hydrogen atoms on the left. In fact, there are four hydrogens and two oxygens on each side of the equation. Atoms are conserved; the equation is balanced.

Note that we could not balance the equation by changing the subscript for oxygen in water.

$$H_2 + O_2 \longrightarrow H_2O_2$$

The equation would be balanced, but it would not mean "hydrogen reacts with oxygen to form *water*." The formula H_2O_2 represents *hydrogen peroxide,* not water. The law of definite proportions tells us that water is always H_2O. We cannot change that merely for the convenience of balancing chemical equations.

Example 5.1 Balance the following equation.

$$N_2 + H_2 \longrightarrow NH_3$$

For this sort of problem we will again find the concept of the least common multiple useful. We'll balance the hydrogen first. There are two hydrogens on the left and three on the right. The least common multiple of 3 and 2 is 6. Six will be the smallest number of hydrogens that can be evenly converted from reactants to products. Thus, we need three molecules of H_2 and two of NH_3.

$$N_2 + 3\ H_2 \longrightarrow 2\ NH_3$$

We've balanced the hydrogens and, in the process, the nitrogens also. There are two on the left and two on the right. The entire equation is balanced!

Example 5.2 Balance the following equation.

$$Fe + O_2 \longrightarrow Fe_2O_3$$

Let's balance oxygen first. The least common multiple is 6. We need three molecules of O_2 and two of Fe_2O_3.

$$Fe + 3\ O_2 \longrightarrow 2\ Fe_2O_3$$

We now have four atoms of iron on the right side. We can get four on the left by placing the coefficient *4* in front of Fe.

$$4\ Fe + 3\ O_2 \longrightarrow 2\ Fe_2O_3$$

The equation is now balanced.

Example 5.3 Balance the following equation.

$$CH_4 + O_2 \longrightarrow CO_2 + H_2O$$

In this equation, oxygen appears in two different products. In this case, we'll leave the oxygen for last and balance the other two elements first. Carbon is already balanced, with one atom on each side of the equation. The least common multiple of 2 and 4 is 4, so to balance hydrogen we place the coefficient *2* in front of H_2O and we have four hydrogens on each side.

$$CH_4 + O_2 \longrightarrow CO_2 + 2\ H_2O$$

Now for the oxygen. There are four oxygens on the right. If we place a *2* in front of O_2, the oxygen will balance.

$$CH_4 + 2\ O_2 \longrightarrow CO_2 + 2\ H_2O$$

The whole equation is balanced.

Example 5.4 Balance the following equation.

$$H_2SO_4 + NaCN \longrightarrow HCN + Na_2SO_4$$

Here we have an equation which involves compounds incorporating complex ions. The SO_4 group should be treated as a unit and balanced as a whole. The same is true of the CN group. As the equation is presently written, the SO_4 groups and the CN groups are balanced, but the hydrogens and the sodiums are not. The least common multiple for sodium is 2, so to get two sodiums on the left we place a *2* before NaCN. The least common multiple for hydrogen is 2, so to get two hydrogens on the right we place a *2* before HCN.

$$H_2SO_4 + 2\ NaCN \longrightarrow 2\ HCN + Na_2SO_4$$

It turns out that these same coefficients balance the CN groups and the SO_4 groups, and the equation as a whole is balanced.

We have made the task of balancing equations deceptively easy. Among the problems facing chemistry majors is that of balancing equations for reactions such as the following.

$$H_2SO_4 + K_2Cr_2O_7 + C_9H_{10} \longrightarrow Cr_2(SO_4)_3 + H_2O + C_7H_6O_2 + CO_2 + K_2SO_4$$

The answer is

$$32\ H_2SO_4 + 8\ K_2Cr_2O_7 + 3\ C_9H_{10} \longrightarrow$$
$$8\ Cr_2(SO_4)_3 + 38\ H_2O + 3\ C_7H_6O_2 + 6\ CO_2 + 8\ K_2SO_4$$

Elaborate schemes have been developed for balancing such equations. Most of you reading this, however, are not going into careers in chemistry, and you will not be faced with balancing so complicated an equation. But you should understand what is meant by a balanced equation and know how to handle simple systems.

5.2 Gases: Gay-Lussac's Law of Combining Volumes

Chemists generally cannot work with individual atoms and molecules. Even the tiniest speck of matter that we can see contains billions of billions

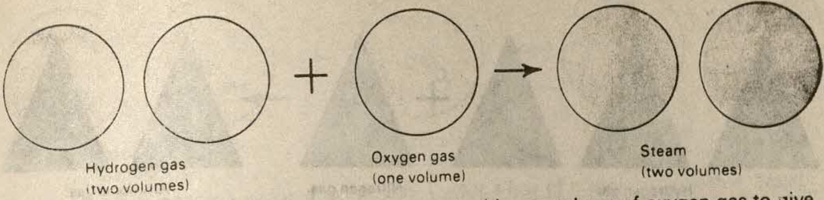


Figure 5.1 Two volumes of hydrogen gas react with one volume of oxygen gas to give two volumes of steam.

of atoms. John Dalton postulated that atoms of different elements had different weights. Therefore, equal weights of different elements would contain different numbers of atoms. Consider the similar situation of golf balls and Ping-Pong balls. A pound of golf balls contains a smaller number of balls than a pound of Ping-Pong balls. One could determine the number of balls in each case simply by counting them. For atoms, however, such a straightforward method is not available. It was in the experiments of a French chemist and the mind of an Italian scientist that approaches to the problem of numbering atoms were found.

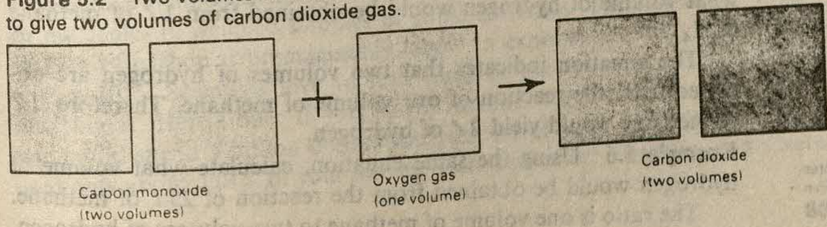
In 1809, Joseph Louis Gay-Lussac announced the results of some chemical reactions that he had carried out with gases. He found that, when all measurements were made at the same temperature and pressure, the volumes of gaseous reactants and products were in a small whole-number ratio. For example, when he allowed hydrogen to react with oxygen to form steam at 100 °C, two volumes of hydrogen would unite with one volume of oxygen to give two volumes of steam (**figure 5.1**). The small whole-number ratio was 2:1:2.

In another experiment (**figure 5.2**), Gay-Lussac found that two volumes of carbon monoxide combined with one volume of oxygen to give two volumes of carbon dioxide (2:1.2).

The ratio is not always 2:1:2. If hydrogen is permitted to react with nitrogen (**figure 5.3**), the product formed is ammonia, and the combining volumes are three of hydrogen with one of nitrogen to give two of ammonia (3:1:2).

Gay-Lussac thought there must be some relationship between the *numbers* of molecules and the volumes of gaseous reactants and products. But it was the Italian chemist Amadeo Avogadro who first explained the *law of combining volumes*. His hypothesis, based on shrewd interpretation of experimental facts, was that equal volumes of all gases (at the same temperature and pressure) contain the same number of molecules. (It was also

Figure 5.2 Two volumes of carbon monoxide gas react with one volume of oxygen gas to give two volumes of carbon dioxide gas.



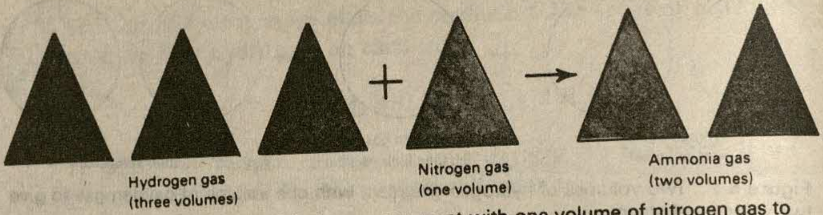


Figure 5.3 Three volumes of hydrogen gas react with one volume of nitrogen gas to give two volumes of ammonia gas.

Avogadro who first suggested that certain elements such as hydrogen, oxygen, and nitrogen were made up of diatomic molecules, i.e., molecules containing two atoms each.)

The equation for the combination of hydrogen and oxygen to form water (steam) is

$$2\ H_2 + O_2 \longrightarrow 2\ H_2O$$

The coefficients of the molecules are the same as the combining ratio of the gas volumes, 2:1:2 (see **figure 5.1**). For the reaction of carbon monoxide and oxygen (see **figure 5.2**), the equation is

$$2\ CO + O_2 \longrightarrow 2\ CO_2$$

The coefficients again reflect the combining volumes. Finally, the formation of ammonia is described in the following equation.

$$3\ H_2 + N_2 \longrightarrow 2\ NH_3$$

The coefficients are identical to the elements of the combining ratio (see **figure 5.3**). The equation says that a nitrogen molecule reacts with three hydrogen molecules to produce two ammonia molecules. It also indicates that if you had 1 million nitrogen molecules, you would need 3 million hydrogen molecules to produce 2 million ammonia molecules. The equation is providing the combining ratios. If identical volumes of gases contain identical numbers of molecules, then, according to the equation, one volume of nitrogen reacts with three volumes of hydrogen to produce two volumes of ammonia.

Example 5.5 According to the equation

$$CH_4 \longrightarrow C + 2\ H_2$$

what volume of hydrogen would be obtained from 1 ℓ of methane (CH_4)?

The equation indicates that two volumes of hydrogen are obtained from the reaction of one volume of methane. Therefore, 1 ℓ of methane would yield 2 ℓ of hydrogen.

Example 5.6 Using the same equation, calculate what volume of hydrogen would be obtained from the reaction of 25 ℓ of methane.

The ratio is one volume of methane to two volumes of hydrogen.

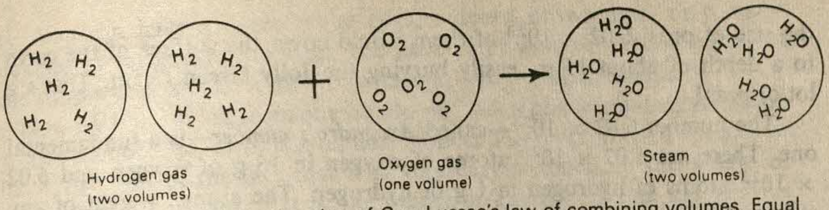


Figure 5.4 Avogadro's explanation of Gay-Lussac's law of combining volumes. Equal volumes of each of the gases contain the same number of molecules.

$$25\ \ell \text{ of methane} \times \frac{2\ \ell \text{ of hydrogen}}{1\ \ell \text{ of methane}} = 50\ \ell \text{ of hydrogen}$$

Example 5.7 Using the same equation, calculate how much methane must have reacted to produce 10 ℓ of H_2.

$$10\ \ell \text{ of } H_2 \times \frac{1\ \ell \text{ of } CH_4}{2\ \ell \text{ of } H_2} = 5\ \ell \text{ of } CH_4$$

5.3 Should Avogadro Get an Unlisted Number?

Recall (chapter 2) that Dalton set up a table of *relative* atomic weights. This table has been modified through the years. The currently accepted relative atomic masses are listed on the inside back cover.

Chemists can't weigh individual atoms or molecules. What they can do to obtain relative weights is weigh *equal numbers* of atoms or molecules of different substances. Avogadro's hypothesis (verified many times through the years) gave chemists a way to do that by measuring the weights of equal volumes of gases.

Once the relative weights of atoms are known, it is possible to plan reactions so no materials are wasted. The relative atomic weight of carbon is 12 (carbon weighs 12 times as much as hydrogen, which is assigned the weight of 1). On this basis, the relative weight of oxygen is 16. If we could (we can't) weigh out 12 amu of carbon and 16 amu of oxygen, we would have one carbon atom and one oxygen atom. From these we could make one molecule of carbon monoxide (CO). If we weigh out 12 g of carbon and 16 g of oxygen, we still have the proper *ratio* of atoms—and these quantities are easily weighed. We would obtain from these amounts of reactants 28 g of CO, with none of the reactants left over. Similarly, if we wished to make carbon dioxide (CO_2), we would weigh out 12 g of carbon and 32 g of oxygen in in order to get exactly 44 g of CO_2. Again, all of the reactants would be consumed in the reaction.

How many carbon atoms are there in 12 g of carbon? Certain techniques have enabled scientists to determine (indirectly) the number of atoms or molecules in weighed samples of some materials. The number of atoms in 12 g of carbon is unimaginably large. In exponential form it is written 6.02×10^{23}. Scientists love to find ways of making very large numbers meaningful. Here's one: if you had a fortune worth 6.02×10^{23} dollars, you could spend a billion dollars each second of your entire life and have used only about .001% of your money. Here's another: if carbon atoms were

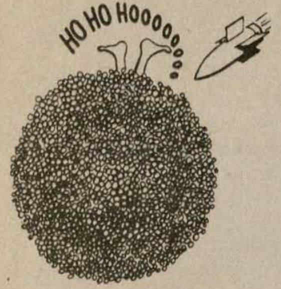


Figure 5.5 The earth, with Jolly Green Giant, covered with 6.02×10^{23} peas.

the size of peas, 6.02×10^{23} of them would cover the surface of the earth to a depth of about 15 m, easily burying the Jolly Green Giant. That's a lot of peas!

The number 6.02×10^{23}—called *Avogadro's number*—is a fundamental one. There are 6.02×10^{23} atoms of oxygen in 16 g of oxygen and 6.02×10^{23} atoms of hydrogen in 1 g of hydrogen. The atomic weight of any element, expressed in grams, contains 6.02×10^{23} atoms.

5.4 Moles of Molecules, Ions, Electrons, Quanta, and Things

If we allow Avogadro's number of carbon atoms to react with Avogadro's number of oxygen *molecules* (each molecule containing two oxygen atoms), we get Avogadro's number of carbon dioxide molecules (**figure 5.6**).

The International Bureau of Weights and Measures has defined the *mole* as one of seven basic SI units. A *mole* is the amount of a substance containing as many elementary units as there are atoms in exactly 12 g of the carbon-12 isotope ($^{12}_{6}C$). The elementary units must be specified by a chemical formula. They may be molecules (such as O_2 or CO_2 or even $C_{24}H_{50}O_4N_5Cl$), they may be atoms (such as C or O), they may be ions (such as SO_4^{2-} or K^+), or they may be pairs of ions (such as NaCl).

Since there are 6.02×10^{23} atoms of carbon-12 in 12 g of the isotope, we may define a mole of carbon dioxide as 6.02×10^{23} molecules of carbon dioxide. A mole of sodium chloride is 6.02×10^{23} ion pairs of sodium chloride, that is, 6.02×10^{23} sodium ions and the same number of chloride ions.

The mole used in chemistry is something like the dozen we use every

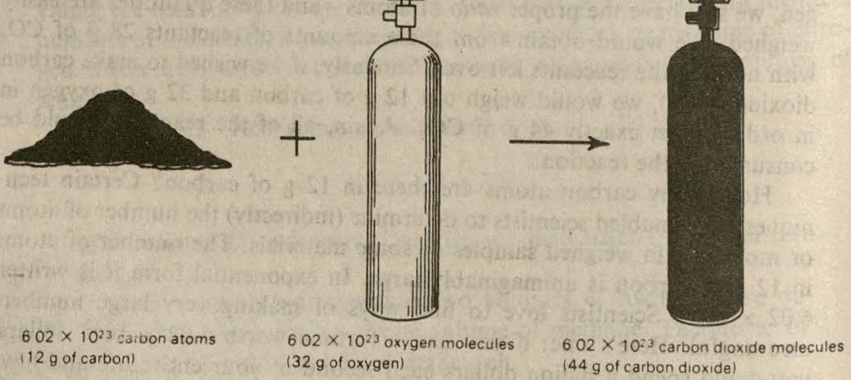

One carbon atom
One oxygen molecule
One carbon dioxide molecule
6.02 × 10^{23} carbon atoms (12 g of carbon)
6.02 × 10^{23} oxygen molecules (32 g of oxygen)
6.02 × 10^{23} carbon dioxide molecules (44 g of carbon dioxide)

Figure 5.6 We can't weigh single atoms or molecules, but we can weigh equal numbers of these fundamental particles.

day. You can have a dozen white eggs, a dozen brown eggs, or a dozen chickens. In each case, you mean you have 12 of whatever you specified. A mole simply means 6.02×10^{23} of whatever you're talking about.

Now 6.02×10^{23} is, from one standpoint, not a pretty number. A million is a nice number; so, also, is a million million. However, the real beauty of 6.02×10^{23} lies in the fact that it is very easy to calculate the weight of this number of particles, that is, the weight of a mole. All one has to do is measure out in grams one formula weight of a substance. The formula weight of a substance is merely the sum of the atomic weights of the atoms in the formula.

Example 5.8 Calculate the formula weight of carbon dioxide (CO_2).

$$1 \times \text{the atomic weight of C} = 1 \times 12 = 12$$

$$2 \times \text{the atomic weight of O} = 2 \times 16 = 32$$

So the formula weight of CO_2 is $12 + 32 = 44$. Thus, 1 mole of CO_2 weighs 44 g.

5.5 Chemical Arithmetic

Chemical equations, therefore, represent not only atom ratios but weight ratios as well. The equation

$$C + O_2 \longrightarrow CO_2$$

tells us that 12 g of carbon react with 32 g of oxygen to give 44 g of CO_2.

We need not use exactly 1 mole of each reactant. The important thing is to keep the ratio constant. For example, in the reaction above the weight ratio of oxygen to carbon is 32:12, or 8:3. We could use 8 g of oxygen and 3 g of carbon to produce 11 g of CO_2. In fact, to calculate the amount of oxygen needed to react with a given amount of carbon, we need only to multiply the amount of carbon by the factor $\frac{32}{12}$.

Example 5.9 Calculate the weight of oxygen needed to react with 10 g of carbon.

$$10\text{ g of C} \times \frac{32\text{ g of } O_2}{12\text{ g of C}} = 27\text{ g of } O_2$$

We can set up conversion factors for any two compounds involved in this reaction. (Conversion factors are reviewed in appendix C.) Typical problems will always ask you to calculate how much of one compound is equivalent to a given amount of one of the other compounds. All you need to do to solve such a problem is put together a conversion factor relating the two compounds. The equation supplies you with the data necessary for constructing the conversion factors. From the equation

$$C + O_2 \longrightarrow CO_2$$

you know that the formula weights of carbon, oxygen gas, and carbon dioxide are, respectively, 12, 32, and 44. The following examples show the derivation of the conversion factors from the formula weights.

Example 5.10 Calculate the weight of carbon that can be burned to carbon dioxide in the presence of 400 g of oxygen. (Hint: You are given the amount of oxygen and are asked for the amount of carbon. You need a conversion factor relating carbon to oxygen.)

$$400 \text{ g of } O_2 \times \frac{12 \text{ g of C}}{32 \text{ g of } O_2} = 150 \text{ g of C}$$

Example 5.11 How many grams of carbon dioxide can be obtained from 48 g of carbon, assuming sufficient oxygen? (Hint: You are given the amount of carbon and are asked for the amount of carbon dioxide. You need a conversion factor relating carbon dioxide to carbon.)

$$48 \text{ g of C} \times \frac{44 \text{ g of } CO_2}{12 \text{ g of C}} = 176 \text{ g of } CO_2$$

Example 5.12 How many grams of carbon are needed to produce 500 g of carbon dioxide? (Hint: You are given the amount of carbon dioxide and are asked for the amount of carbon. You need a conversion factor relating carbon to carbon dioxide.)

$$500 \text{ g of } CO_2 \times \frac{12 \text{ g of C}}{44 \text{ g of } CO_2} = 136 \text{ g of C}$$

5.6 Burrowing Through: The Mole Method

The examples of the previous section were based on a very simple reaction. In the balanced equation, there were no coefficients other than 1. That is, one molecule of oxygen reacted with one carbon atom to produce one carbon dioxide molecule. When a balanced equation does involve coefficients other than 1, that fact introduces a slight complication into the calculation. There are a number of ways of dealing with this complication. We shall illustrate the *mole method*, which is probably the most versatile. In principle we are doing the same thing we did in section 5.5, only now we are going to get a mole ratio instead of a gram ratio from the chemical equation.

Before we work with an equation, let's try a conversion between moles and grams for a single compound.

Example 5.13 Your friendly neighbor, an alchemist, is working on a secret solution. In response to your offer to help he asks you to weigh out 0.5 mole of ammonium sulfate [$(NH_4)_2SO_4$]. How many grams would you weigh out?

Calculate the formula weight first, remembering that "$(NH_4)_2$" means that everything within the parentheses should be multiplied by 2.

2 × the atomic weight of N = 2 × 14 = 28
8 × the atomic weight of H = 8 × 1 = 8

$$1 \times \text{the atomic weight of S} = 1 \times 32 = 32$$
$$4 \times \text{the atomic weight of O} = 4 \times 16 = 64$$

So the formula weight of $(NH_4)_2SO_4$ is $28 + 8 + 32 + 64 = 132$, and

$$1 \text{ mole of } (NH_4)_2SO_4 = 132 \text{ g of } (NH_4)_2SO_4$$

Now you have the conversion factor to use in your calculation.

$$0.5 \text{ mole} \times \frac{132 \text{ g of } (NH_4)_2SO_4}{1 \text{ mole of } (NH_4)_2SO_4} = 66 \text{ g}$$

Now we're ready to tackle an equation. We shall work out the sort of problem industrial chemists face every day. Whether chemists are making drugs, obtaining metals from their ores, synthesizing plastics, or whatever, they must use materials economically. The mole is the method.

Example 5.14 Ammonia (for fertilizer and other uses) is made by causing hydrogen and nitrogen to react at high temperature and pressure. The equation (not balanced) is

$$N_2 + H_2 \longrightarrow NH_3$$

How many grams of ammonia can be made from 60 g of hydrogen?

First, we must balance the equation (see example 5.1).

$$N_2 + 3\,H_2 \longrightarrow 2\,NH_3$$

Next, we calculate the formula weights of the compounds involved in the problem, that is, of hydrogen and ammonia.

$$H_2 \text{ weighs } 2$$
$$NH_3 \text{ weighs } 17$$

We are given an amount of hydrogen and are asked for a weight of ammonia. We must convert the weight given to moles.

$$60 \text{ g of } H_2 \times \frac{1 \text{ mole of } H_2}{2 \text{ g of } H_2} = 30 \text{ moles of } H_2$$

Next, we must use the coefficients given in the equation to determine the number of moles of ammonia that can be obtained from the calculated moles of hydrogen gas. The equation tells us that 3 moles of H_2 produce 2 moles of NH_3. Thus,

$$30 \text{ moles of } H_2 \times \frac{2 \text{ moles of } NH_3}{3 \text{ moles of } H_2} = 20 \text{ moles of } NH_3$$

Finally, we must convert moles of ammonia to grams of ammonia.

$$20 \text{ moles of } NH_3 \times \frac{17 \text{ g of } NH_3}{1 \text{ mole of } NH_3} = 340 \text{ g of } NH_3$$

Or we could do it all in one step.

$$60 \text{ g of } H_2 \times \frac{1 \text{ mole of } H_2}{2 \text{ g of } H_2} \times \frac{2 \text{ moles of } NH_3}{3 \text{ moles of } H_2} \times \frac{17 \text{ g of } NH_3}{1 \text{ mole of } NH_3} = 340 \text{ g of } NH_3$$

The sequence of steps to be followed in the mole method is:

1. Balance the equation.
2. Determine the formula weights of materials of interest.
3. Calculate number of moles from the number of grams *given* and the formula weight.
4. Calculate (using the ratio specified by the equation) the number of moles of the compound you were asked about from the number of moles calculated in step 3.
5. Finally, convert the number of moles determined in step 4 to the weight in grams, using the appropriate formula weight.

Example 5.15 How many grams of oxygen must be consumed if the following reaction is to produce 9 g of water?

$$H_2 + O_2 \longrightarrow H_2O$$

The balanced equation is

$$2\,H_2 + O_2 \longrightarrow 2\,H_2O$$

The formula weight for oxygen gas is 32, and the formula weight for water is 18.

$$9 \text{ g of } H_2O \times \frac{1 \text{ mole of } H_2O}{18 \text{ g of } H_2O} \times \frac{1 \text{ mole of } O_2}{2 \text{ moles of } H_2O} \times \frac{32 \text{ g of } O_2}{1 \text{ mole of } O_2} = 8 \text{ g of } O_2$$

Structure, Stability, and Spontaneity

We saw at the beginning of chapter 4 that some electronic configurations are more stable than others. Sodium *ions* and chloride *ions*, arranged in a crystal lattice, are less reactive than sodium *atoms* and chlorine *molecules*. We do know that if sodium metal and chlorine gas are mixed, a vigorous reaction ensues.

$$2\,Na + Cl_2 \longrightarrow 2\,NaCl$$

A great deal of energy as heat and light is produced during the reaction. Sometimes this energy is listed as one of the products in the chemical equation.

$$2\,Na + Cl_2 \longrightarrow 2\,NaCl + \text{energy}$$

Energy changes associated with a particular reaction are quantitatively related to the *amount* of chemicals changed. For example, burning 16 g (1 mole) of methane to form carbon dioxide and water releases 192 kcal of energy as heat.

$$CH_4 + 2\ O_2 \longrightarrow CO_2 + 2\ H_2O + 192\ \text{kcal}$$

When this information is included in the equation, it is possible to calculate the amount of heat produced from a certain amount of reactant in much the same way as weights of material products are calculated.

Example 5.16 The reaction between hydrogen and chlorine to form hydrogen chloride gas results in the release of 44 kcal of heat per mole of hydrogen consumed.

$$H_2 + Cl_2 \longrightarrow 2\ HCl + 44\ \text{kcal}$$

How much heat would be released by the reaction of 40 g of hydrogen with chlorine?

First, calculate the number of moles of hydrogen, using the formula weight.

$$40\ \text{g of}\ H_2 \times \frac{1\ \text{mole of}\ H_2}{2\ \text{g of}\ H_2} = 20\ \text{moles of}\ H_2$$

Then, using the information given by the equation, calculate the heat produced.

$$20\ \text{moles of}\ H_2 \times \frac{44\ \text{kcal}}{1\ \text{mole of}\ H_2} = 880\ \text{kcal}$$

Or

$$40\ \text{g of}\ H_2 \times \frac{1\ \text{mole of}\ H_2}{2\ \text{g of}\ H_2} \times \frac{44\ \text{kcal}}{1\ \text{mole of}\ H_2} = 880\ \text{kcal}$$

Chemical reactions which result in the release of heat are said to be *exothermic*. The burning of methane is an exothermic reaction, as is the burning of gasoline or coal. In each case, chemical energy is converted into heat energy. There are other reactions, such as the decomposition of water, for which energy must be supplied.

$$2\ H_2O + 137\ \text{kcal} \longrightarrow 2\ H_2 + O_2$$

If the energy is supplied as heat, such reactions are said to be *endothermic*. It takes 137 kcal of energy to decompose 36 g (2 moles) of water into hydrogen and oxygen. It should be noted that the same amount of energy is released when enough hydrogen is burned to form 36 g (2 moles) of water.

$$2\ H_2 + O_2 \longrightarrow 2\ H_2O + 137\ \text{kcal}$$

The energy released in an exothermic reaction is related to the *chemical energy* present in the reactants. This energy is a form of *potential energy.* Potential energy is released (as heat or light, for example) when reactants are brought together in a way that allows them to achieve more stable electronic arrangements.

To say that a reaction is exothermic does not necessarily mean that it is spontaneous. For example, coal (carbon) has a lot of chemical energy. Carbon reacts with oxygen to form carbon dioxide with the release of considerable heat. But coal doesn't react very rapidly with oxygen at ordinary temperatures. In fact, one can store a pile of coal in air indefinitely without perceptible change. Before coal will react with oxygen to release its stored energy, it must be heated to a temperature of several hundred degrees. The coal must be supplied with a certain amount of energy (called the *energy of activation*) before it will begin to burn steadily. Once this energy of activation is supplied, the heat evolved in the reaction will keep the coal burning brightly, and the energy eventually produced will exceed the amount of energy required to start the reaction. Overall, you get more energy out than you put in. The reaction is exothermic. In an endothermic reaction, more energy goes in than comes out.

We will return to the burning of coal in a moment, but first let's consider an analogy involving a more familiar situation. If you were in Browning, Montana (elevation 1300 m), and wished to travel to Kalispell (elevation 900 m), you could choose to drive the scenic Going-to-the-Sun Highway through Glacier National Park. To do this you would have to cross the continental divide at Logan Pass (elevation 2000 m). First, you would have to climb 700 m, but then it would be downhill the rest of the way (**figure 5.7**).

The reaction of coal (carbon) with oxygen can be explained in much the same way. The reactants, carbon and oxygen, lie in a rather high potential energy valley (**figure 5.8**). A certain amount of energy has to be put into the system for it to get over the top of the "mountain." Once the reaction is under way, the heat released more than compensates for the energy needed to get the reaction going in the first place.

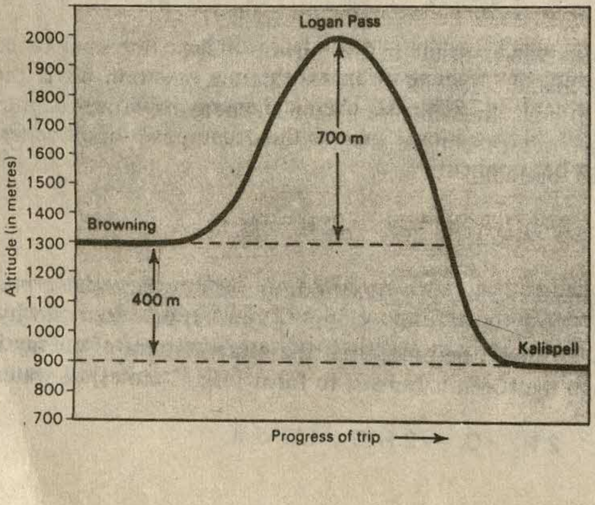


Figure 5.7 To get from Browning Montana to Kalispell via Going-to-the-Sun Highway, we would first have to climb to Logan Pass, even though Kalispell is 400 m lower in elevation than Browning.

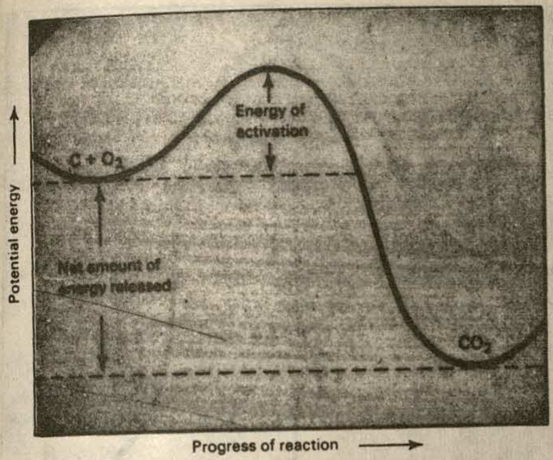


Figure 5.8 To get from reactants (carbon and oxygen) to product (carbon dioxide), we must first put some energy into the system.

5.8 Reversible Reactions: Forward and Backward

Living cells take in oxygen and "burn" glucose to obtain energy.

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + \text{energy}$$

Glucose

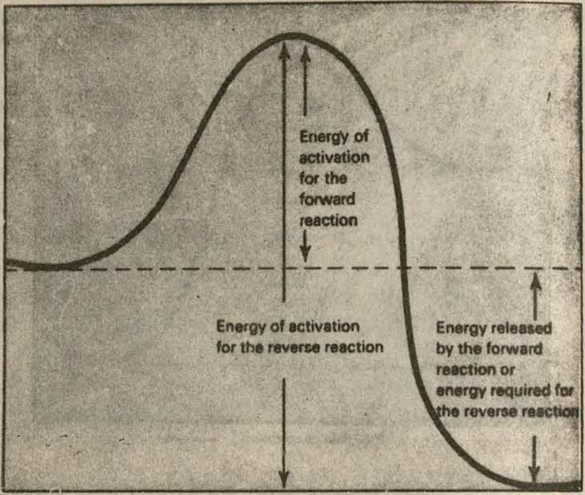
Green plants carry out the reverse reaction (an endothermic reaction called *photosynthesis*), using energy from sunlight to convert carbon dioxide and water to glucose and oxygen.

$$6\ CO_2 + 6\ H_2O + \text{energy} \rightarrow C_6H_{12}O_6 + 6\ O_2$$

All life on our planet is based on this *reversible* reaction. But what makes it go one way in one case and the opposite way in another? One obvious answer is energy. Since energy is released when glucose is oxidized, the reactants (glucose and oxygen) must be at a higher energy level than the products (carbon dioxide and water). As we have indicated previously, this does not mean that the path is straight downhill from reactants to products. Indeed, if glucose and oxygen are mixed at ordinary temperatures outside a cell, no perceptible reaction occurs. As with the reaction of coal and oxygen, which we cited before, a certain amount of energy, the energy of activation, must be supplied before the reaction takes place. The potential energy diagram for this reaction (**figure 5.9**) strongly resembles that for the coal and oxygen reaction (see **figure 5.8**).

For reversible reactions, the energy hill, or the barrier to reaction, may be approached from either side. That is, one can read the diagram from left to right or right to left. With the burning of glucose, one is considering an exothermic reaction in which higher-energy reactants are converted to lower-energy products. When read in the reverse direction, the diagram presents the energy changes which occur in the endothermic reaction called photosynthesis. The climb to the top of the barrier (the activation energy) is longer from one side than from the other. The activation energy is the

Figure 5.9 Potential energy diagram for a reversible reaction.


Energy of activation for the forward reaction
Energy of activation for the reverse reaction
Energy released by the forward reaction or energy required for the reverse reaction

difference in energy between the level the reactants are on and the top of the energy hill. When the reactants are in the valley at the left (as in the forward reaction), the climb to the top is not so high. When the reactants are in the valley to the right (as in the reverse reaction), the climb to the top is much longer. The potential energy diagram shown here is much simplified. Just as one seldom crosses a mountain by going straight up one side and straight down the other, reactions seldom proceed by a smooth, one-hump potential energy change.

5.9 Reaction Rates: Collisions, Orientation, and Energy

Before atoms, molecules, or ions can react, they must first get together: they must collide. Second, for all except the simplest particles, they must come together in the proper orientation. Third, the collision must provide a certain minimum energy, which we have called the activation energy.

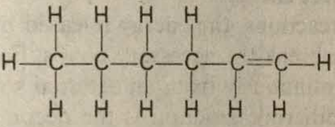
First, let's consider the frequency of collision, which is influenced by two factors, concentration and temperature. The more concentrated the reactants, the more frequently the particles will collide, simply because there are more of them in a given volume. Molecules also move faster at higher temperatures; thus, an increase in temperature also increases the frequency of collision. The effects of concentration and temperature on reaction rates will be discussed in more detail in following sections.

Now, though, let's take a closer look at the effect of orientation. It might not be obvious that orientation is important. Sometimes, though rarely, it's not. Consider a situation in which you want to knock someone down. You can tackle from the front, back, or side and still accomplish your objective. If, however, a kiss is the objective, then an orientation in which the participants are face to face works best. For chemical reactions, there are also a few instances in which orientation is not important. If two hydrogen atoms are to react to form a hydrogen molecule,

$$2\,H \rightarrow H_2$$

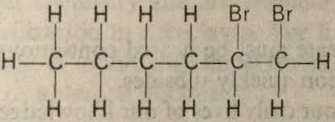
then orientation is unimportant. The quantum mechanical view of hydrogen atoms depicts them as symmetrical (spherical) electron clouds. Front, back, top, and bottom all look the same. Therefore all orientations of two hydrogen atoms are identical. If they come into contact with one another, they will react.

For most particles, however, proper orientation is a prerequisite to reaction. Consider the molecule



$$\mathrm{H{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{C}{=}\underset{H}{C}{-}H}$$

The two carbon atoms sharing the double bond can react with bromine to form



$$\mathrm{H{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{Br}{C}}{-}\underset{H}{\overset{Br}{C}}{-}H}$$

Now, it is possible for bromine to strike the original compound anywhere along its length. However, only if the collision occurs in such a way as to bring bromine into contact with the electrons in the double bond will the reaction occur. It is even true that the bromine must approach the electrons of the double bond from a certain direction. Here is a case in which orientation is very important. We shall point out another example of proper orientation shortly.

The third factor, that collisions must provide a certain minimum energy, is a good deal more subtle. There is a temperature effect which will be discussed in some detail in the next section. Certain substances, called catalysts, may substantially lower this activation energy, thus increasing the reaction rate. The effect of catalysts will be discussed more thoroughly in section 5.11.

5.10 Getting There Faster: The Effect of Temperature

Reactions generally take place at a faster rate when temperatures are high. We have seen that carbon reacts very slowly with oxygen at room temperature. When heated, the coal reacts much faster. The effect of temperature on the rates of chemical reactions is explained by the kinetic-molecular theory. We shall consider this theory in more detail in the next chapter. For the moment, we will cite one of its postulates, which states that, at high temperatures, molecules move more rapidly. Thus, they collide more frequently, providing increased chance for reaction.

At high temperatures, the rapidly moving molecules also strike one another harder. The harder these collisions are, the more energy is involved in them. These harder collisions are more likely to supply the activation energy needed to break the chemical bonds and get the reaction going. Consider the reaction which takes place between hydrogen gas and chlorine gas.

In order for hydrogen and chlorine to react, bonds between hydrogen atoms and between chlorine atoms must be broken.*

$$\mathrm{H{-}H + Cl{-}Cl \longrightarrow 2\ H{-}Cl}$$

This is an exothermic reaction. Once it has started, the energy released by the formation of hydrogen-to-chlorine bonds more than compensates for that required to break H—H and Cl—Cl bonds. There is a net conversion of chemical energy to heat energy.

In endothermic reactions, the energy released by bond formation is less than that required to break the necessary bonds. For these reactions, energy must be supplied continuously from an external source, or the process will stop. A typical endothermic reaction is the decomposition of a salt called potassium chlorate ($KClO_3$) to give oxygen and another salt, potassium chloride (KCl).

$$\mathrm{2\ KClO_3 + heat \longrightarrow 2\ KCl + 3\ O_2}$$

The potassium chlorate must be heated continuously. If the source of heat is removed the reaction quickly subsides.

Figure 5.10 Heart surgery is often performed with the patient's temperature lowered to slow metabolic processes and thus minimize the possibility of brain damage. (Courtesy of the University of Illinois Medical Center, Chicago.)

We make use in our daily lives of our knowledge of the effect of temperature on chemical reactions. For example, we freeze foods to retard those chemical reactions that lead to spoilage. On the other hand, if we want to cook our food more rapidly, we turn up the heat. There is a general rule of thumb that reaction rates double for every temperature increase of 10 °C. (There are many exceptions to this rule, and it should be applied only if there are no other data available.) The chemical reactions which occur in our bodies generally do so at a constant temperature of 37 °C (98.6 °F). A few degrees' rise in temperature (fever) leads to an increase in respiration, pulse rate, and other physiological reactions. A drop in body temperature of a few degrees slows these same processes considerably, as is exemplified by the slowed metabolism of hibernating animals. Use is made of this phenomenon in some surgical procedures. In some cases of heart surgery, the body temperature of the patient is lowered to about 15 °C (60 °F). Ordinarily, the brain is permanently damaged when its oxygen supply is interrupted for more than 5 minutes. But at the lower temperature metabolic processes slow considerably and the brain may survive much longer periods of oxygen deprivation. The surgeon can stop the heartbeat, perform an hour-long surgical procedure on the heart, and then restart the heart and bring the patient's temperature back to normal.

It must be said that, despite these examples, the manipulation of reaction rates in living systems through changes in temperature is severely restricted. Increasing temperature, for example, may "kill" enzymes (section

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*This statement says nothing about the *order* in which the bonds are broken. This sequence, called the mechanism of a reaction, can be quite complicated (see p. 123).

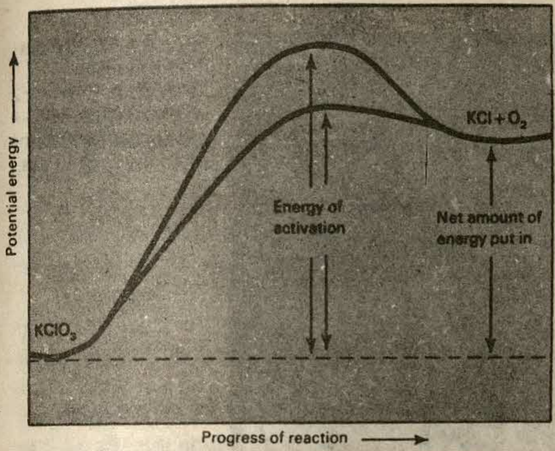

Figure 5.11 The decomposition of potassium chlorate is endothermic. A catalyst acts to lower the energy of activation (colored line) compared to that required for the uncatalyzed reaction.

5.11) that moderate cellular chemistry and are absolutely essential to life. We kill germs by heat sterilization in autoclaves. For living cells, there is often a rather narrow range of optimum temperatures. Both higher and lower temperatures can be disabling, if not deadly.

5.11 Getting There Faster: Catalysis

Recall the endothermic reaction involving the decomposition of potassium chlorate to oxygen and potassium chloride (p. 120). For the oxygen to be produced at a useful rate, the potassium chlorate must be heated to over 400 °C. However, if we add a small amount of manganese dioxide (MnO_2), we can get the same rate of oxygen evolution by heating the reactant to just 250 °C. Further, after the reaction is complete, the manganese dioxide can be completely recovered, unchanged. A substance which, like manganese dioxide, changes the rate of a chemical reaction without itself being changed is called a *catalyst.* In general, catalysts act by lowering the activation energy required for the reaction to occur (**figure 5.11**). If activation energy is lower, then the collisions of more slowly moving molecules will be sufficient to supply that energy. The lower temperature required for a catalyzed reaction reflects this. This energy of activation is lowered because the catalyst changes the *path* of the reaction. To return to our analogy of the trip from Browning to Kalispell, it is possible to take an alternate route. U.S. Highway 2 crosses the continental divide through Marias Pass. This route involves a climb of only 300 m, compared to 700 m via Logan Pass (**figure 5.12**). This alternate route is analogous to that provided by a catalyst in a chemical reaction.

Catalysts are of great importance in chemical industry. A reaction which would otherwise be so slow as to be impractical can be made to proceed at a reasonable rate with the proper catalyst.

Catalysts are even more important in living organisms, where raising the temperature by 100 °C is not a feasible way of increasing the rate of critical reactions. If we raised our body temperature by 100 °C, we'd boil our blood, among other things, and our fatty tissue would melt (though that might not

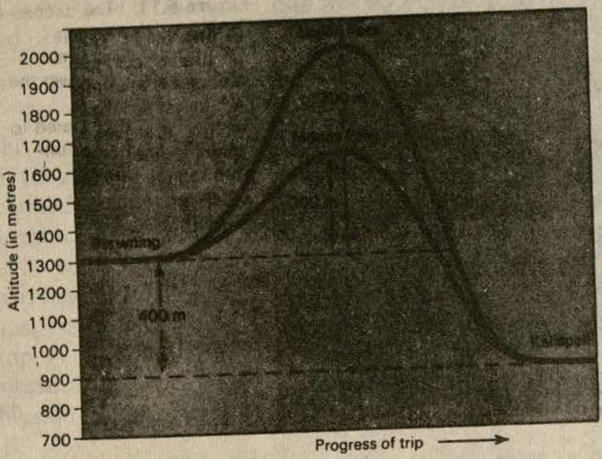

Figure 5.12 To get from Browning to Kalispell via Highway 2 involves a lower energy barrier than the route via Logan Pass.

be undesirable). Biological catalysts, called *enzymes*, mediate nearly all the chemical reactions that take place in living systems. But these catalysts themselves may suffer irreversible damage when living cells are subjected to too high a temperature. Once a catalyst is deactivated, the reactions which required the catalyst no longer proceed at a rate which maintains life. In addition to being examples of catalysts, enzymes offer a striking illustration of the importance of orientation in chemical reactions. These compounds are huge molecules, each possessing what is called an active site. The reactants must come into contact with this active site if the enzyme is to catalyze the reaction. If the reactants do not collide at the active site, no reaction occurs. So important are enzymes to life that we shall discuss them more fully in chapter 26.

5.12 Getting There Faster: Increasing the Concentration

Another factor affecting the rate of a chemical reaction is the concentration of reactants. The more reactant molecules there are in a volume of space, the more collisions will occur. The more collisions there are, the more reactions will occur. For example, you can light a wood splint and then blow out the flame. The splint will continue to glow as the wood reacts slowly with the oxygen of the air. If the glowing splint was placed in pure oxygen, the splint would burst into flame, indicating a much more rapid reaction. This more rapid reaction can be interpreted in terms of the concentration of oxygen. Air is about one-fifth oxygen. The concentration of O_2 molecules in pure oxygen is, therefore, about five times as great as in air. The caution against smoking in a hospital room where a patient is in an oxygen tent is not merely a concession to the sensitivity of nonsmokers. It is meant to prevent disaster.

For reactions in solution, the concentration of a reactant can be increased if more of it is dissolved. One of the first studies of reaction rates was done by Ludwig Wilhelmy in 1850. He studied the rate of reaction of sucrose (cane or beet sugar) with water. The products are two simpler sugars, glucose and fructose.

$$\text{Sucrose} + H_2O \xrightarrow{HCl} \text{glucose} + \text{fructose}$$

(We will not be concerned with the chemical formulas for these sugars at this time. The hydrochloric acid serves as a catalyst for the reaction. Chemists generally write formulas or names for catalysts above the arrow, since the catalyst is recovered unchanged.) Wilhelmy found that the rate of the reaction was proportional to the concentration of sucrose. If he dissolved 0.001 mole of sucrose in 1 ℓ of water, the sucrose reacted at a certain rate. If he doubled the concentration of sucrose (i.e., if he dissolved 0.002 mole/ℓ of water), the reaction rate was doubled.

In general, when the temperature is constant and the catalyst (if any) is present in fixed amount, the rate of the reaction can be related quantitatively to the amounts of reacting substances. The relationship is not necessarily a simple one, however. In order to know *which* reacting substances are involved in determining the rate, one must know the step-by-step detail of how the molecules collide, come apart, and recombine.

Consider again the photosynthesis reaction.

$$6\ CO_2 + 6\ H_2O + \text{energy} \rightarrow C_6H_{12}O_6 + 6\ O_2$$

For this reaction to occur in one step, six carbon dioxide molecules and six water molecules would all have to come together at the same instant in an effective collision. Such an event is highly unlikely. In fact, even three-body collisions are rare. Most reactions proceed through a series of steps involving collisions of only two molecules each. Some steps may involve only the breaking of a bond of a single molecule. The photosynthesis reaction involves an extraordinarily complex web of intermediate steps, but each individual step is fairly simple. Virtually all steps require enzymes as catalysts.

The step-by-step process, or *mechanism,* by which a reaction takes place is determined by a study of the rate of the reaction as various factors, such as temperature, concentrations, and catalysts, are changed. Such studies are important in chemistry, for chemists want to get as much product as possible with a minimum expenditure of materials and energy. Investigations of mechanisms are also important in the chemistry of living cells. Many types of cancer are thought to be induced by chemicals. A lot of research is under way to work out the mechanism by which the chemicals act—or are acted upon—in the induction of cancer. A knowledge of the mechanism of various metabolic reactions has enabled scientists to determine how certain poisons work, and this knowledge has led to effective treatments in many instances. Certain diseases of genetic origin involve the disruption of a single step in the mechanism of a reaction essential to health. Again, this information has permitted physicians to deal successfully with what might otherwise have been a fatal defect.

5.13 Equilibrium in Chemical Reactions

For reversible reactions, those which proceed in both a forward and a backward direction, the concept of rate requires further consideration. In such reactions, the reverse reaction can't occur until some product molecules (that is, product with respect to the forward reaction) have been formed. Even then, because of the effect of concentration on rate, the reverse reaction will be slow until sufficient product has been formed to increase the chance of these molecules getting together to form reactants once more. Similarly, as the reactants change to products, there will be fewer collisions between reactant molecules, because their number becomes depleted. In isolated systems (ones that are cut off from outside influences) the rates of the forward and reverse reactions eventually become equal, and a condition called *equilibrium* is established. At equilibrium there *appears* to be no further reaction. In this case appearances are deceiving. Reactants are still changing to products and products are still changing back to reactants. It is just that these changes are occurring at precisely the same rate. For every reactant molecule lost through the forward reaction, one is gained through the reverse reaction. Once equilibrium is established, we can measure no change in the concentration of reactants or products. Because molecules are still reacting, even though their concentrations don't change, we say that equilibrium is a dynamic situation.

Equilibrium, we mentioned, is established for reversible reactions in isolated systems, those for which external conditions such as temperature and pressure do not change. What happens if those external conditions do change? For the answer to that question we shall once again use as an example the reaction of nitrogen and hydrogen to form ammonia.

$$N_2 + 3\,H_2 \rightleftharpoons 2\,NH_3 + \text{energy}$$

The double arrow indicates that this is a reversible reaction. All of the compounds involved in this reaction are gases. From the work of Gay-Lussac and Avogadro we know that the coefficients given in the equation reflect the combining volumes of the gases. The reactants occupy four volumes and the products two. In chapter 6 we shall study the effects of temperature and pressure on the volume of a gas. For the moment, let us just say that increased pressure tends to reduce the volume of a gas. If the pressure of the equilibrium system we are considering is increased, the equilibrium will be disrupted and the rate of the forward reaction will increase. This has the effect of changing reactants which occupy four volumes to products which occupy only two. Thus, the total volume of the system will decrease. If the pressure is held constant at the new, higher value, equilibrium will again be established. But in the new equilibrium the concentration of ammonia (NH_3) will be higher than it was before the pressure changed. We sometimes describe this change by saying that the equilibrium has been shifted to the right. Thus, for the reversible reaction of nitrogen and hydrogen, an increase in pressure shifts the equilibrium to the right.

Observations of changes that occur in an equilibrium system when factors such as concentration, pressure, or temperature are changed were made in the 19th century. These effects were summarized in 1884 by a French chemist, Henri Louis Le Chatelier. His rule, still called *Le Chatelier's principle,* may be stated as follows. If a stress is applied to a system at equilibrium, the system rearranges in such a direction as to minimize the stress. If heat is added to the N_2—H_2—NH_3 system, the reaction will proceed to the left, using up heat (energy). If more nitrogen gas is added to the system, the reaction will go to the right, using up nitrogen. If additional hydrogen gas is introduced, the system will shift to the right, to use up hydrogen. Additional ammonia will cause the reaction to proceed to the left, using up ammonia.

The equilibrium can also be shifted by removal of one of the substances. Removal of ammonia will cause hydrogen and nitrogen to react, forming more ammonia. Removal of hydrogen will cause ammonia to break down and form more hydrogen (and, incidentally, more nitrogen). It should be noted, however, that a catalyst will not shift an equilibrium system. Catalysts change the rate of both the forward and reverse reactions. They do not change the position of the equilibrium, that is, the equilibrium concentrations of reactants and products.

In chapter 7, we shall discuss equilibria between liquid and solid phases and between liquid and vapor phases. In chapter 9, we shall encounter equilibria involving solutions. The importance of this concept cannot be overemphasized. Life itself can be viewed as an equilibrium. Some molecules are broken down and some are put together. Health is that state in which the two processes are properly balanced.

Problems

1. Balance the following chemical equations.
   a. $Al + O_2 \rightarrow Al_2O_3$
   b. $C + O_2 \rightarrow CO$
   c. $N_2 + O_2 \rightarrow NO$
   d. $SO_2 + O_2 \rightarrow SO_3$
   e. $NO + O_2 \rightarrow NO_2$
   f. $Zn + HCl \rightarrow ZnCl_2 + H_2$
   g. $Al_2(SO_4)_3 + NaOH \rightarrow Al(OH)_3 + Na_2SO_4$
   h. $Zn(OH)_2 + HNO_3 \rightarrow Zn(NO_3)_2 + H_2O$
   i. $NH_4OH + H_3PO_4 \rightarrow (NH_4)_3PO_4 + H_2O$
2. Calculate the formula weight (to the nearest whole number) for each of these compounds.
   a. CH_4
   b. AlF_3
   c. NH_4NO_3
   d. $Ca(NO_3)_2$
   e. $BaSO_4$
   f. UF_6
   g. $Mg(OH)_2$
   h. H_3PO_4
   i. $KClO_3$
   j. $(NH_4)_2SO_4$
3. Calculate the number of moles in each of the following samples.
   a. 32 g of CH_4
   b. 336 g of AlF_3
   c. 8.0 g of NH_4NO_3
   d. 1.64 g of $Ca(NO_3)_2$
   e. 0.233 g of $BaSO_4$
   f. 17.6 g of UF_6
   g. 5.8 g of $Mg(OH)_2$
   h. 980 g of H_3PO_4
   i. 3.69 g of $KClO_3$
   j. 0.0132 g of $(NH_4)_2SO_4$
4. Calculate the number of grams in each of these samples.
   a. 0.001 mole of CH_4
   b. 6 moles of AlF_3
   c. 0.05 mole of NH_4NO_3
   d. 1.5 moles of $Ca(NO_3)_2$
   e. 3 moles of $BaSO_4$
   f. 40 moles of UF_6
   g. 5.8 moles of $Mg(OH)_2$
   h. 10 moles of H_3PO_4
   i. 0.02 mole of $KClO_3$
   j. 0.25 mole of $(NH_4)_2SO_4$
5. Consider the reaction

$$S + O_2 \rightarrow SO_2$$

a. How many moles of SO_2 would be formed by the burning of 4 moles of sulfur?
b. How many grams of SO_2 would be formed by the burning of 8 g of sulfur?
c. How much sulfur would be needed to produce 3.2 g of SO_2?
d. Under the same conditions of temperature and pressure, what volume of O_2 would be consumed in the production of 10 ℓ of SO_2?

6. Consider the reaction

$$CH_4 + 2\ O_2 \longrightarrow CO_2 + 2\ H_2O + 192\ \text{kcal}$$

a. How many grams of O_2 are required to react completely with 8 g of CH_4?
b. How much energy would be produced under the conditions described in question a?

7. Define or illustrate each of the following.

a. energy of activation	f. mole
b. catalyst	g. Avogadro's number
c. exothermic	h. reversible reaction
d. endothermic	i. equilibrium
e. formula weight	j. Le Chatelier's principle

8. Why does raising the temperature generally increase the rate of a reaction? Why does increasing the concentration of the reactants generally do the same?
9. Predict the effect of increased pressure and then of increased temperature on each of the following equilibria.
   a. $3\ O_2(g) \rightleftarrows 2\ O_3(g) + \text{heat}$
   b. $N_2(g) + 3\ H_2(g) \rightleftarrows 2\ NH_3(g) + \text{heat}$
   c. $2\ CO_2(g) + \text{heat} \rightleftarrows 2\ CO(g) + O_2(g)$
10. The Haber process for making ammonia is given in the equation in problem 9b. What would be the effect of each of the following on the equilibrium of that reaction?

a. the removal of ammonia	c. the removal of heat
b. the addition of nitrogen	d. the addition of a catalyst

11. Explain how the orientation of reactants can influence the rate of a reaction.
12. What is the "mechanism" of a reaction?

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chapter 6

Gases

We have seen firsthand the barren, airless moon. We have photographed the desolation of Mercury from a few kilometres up. Our spaceships have measured the inhospitably high temperatures of Venus and have given us a closeup portrait of the crushing atmosphere of Jupiter. Our experiments on the harsh Martian surface failed to confirm the presence of life there. Perhaps we will come at last, in the final decades of the 20th century, to realize that Earth is a small island of green and blue in the vastness of space. And perhaps we will come to treat the earth with the love and care that it deserves as the only homeland we will ever know.

The life-support system of Spaceship Earth consists in part of a thin blanket of gases called the atmosphere. It is difficult to measure just how deep the atmosphere is. It does not end abruptly, but gradually fades as the distance from the surface of the earth increases. We do know, though, that 99% of the atmosphere lies within 30 km (19 mi) of the surface of the earth. That thin layer of air—which, if the earth and its atmosphere were an apple, would be thinner than the peel—is all that stands between us and the emptiness of space. Our supply of air, once thought inexhaustible, now appears limited.

Air is so familiar, and yet so nebulous, that it is difficult to think of it as matter. But it is matter—matter in the gaseous state. All gases, air included, have mass and occupy space. Like other forms of matter, gases obey certain physical laws. In this chapter we will examine some of those laws and see how they are related to certain vital processes—such as breathing!

6.1 Air: A Mixture of Gases

Air is a mixture of gases. Dry air is (by volume) about 78% nitrogen (N_2), 21% oxygen (O_2), and 1% argon (Ar). The amount of water vapor varies up to about 4%. There are a number of minor constituents, the most important of which is carbon dioxide (CO_2). The concentration of carbon

Table 6.1
Composition of the earth's dry atmosphere
(in molecules of each substance per 10 000 molecules)

Substance	*Formula*	*Number of Molecules*
Nitrogen	N_2	7800
Oxygen	O_2	2100
Argon	Ar	93
Carbon dioxide	CO_2	3
All others	—	4
Total		10 000

dioxide in the atmosphere is believed to have increased from 296 parts per million (ppm) in 1900 to its present value of 318 ppm. It will most likely continue to rise as we burn more and more fossil fuels (coal, oil, and gas). The composition of the atmosphere is summarized in **table 6.1.**

Air is a mixture of gases, but what are gases? Perhaps they are best understood in terms of the kinetic-molecular theory.

6.2 The Kinetic-Molecular Theory

We have mentioned the kinetic-molecular theory previously. Now we are going to go into more detail in order to give you some idea of how this model enables scientists to visualize gases (and liquids and solids) and to understand the changes that occur in these materials.

The theory treats gases as collections of individual particles in rapid motion (hence the term *kinetic*). The particles of nitrogen gas, for example, are molecules (N_2); those of argon gas (Ar) are atoms. The distances between the particles are very large when compared to the dimensions of the particles themselves. This fact explains why gases, by comparison with solids and liquids, can so readily be compressed. According to the theory, the individual particles of a solid or liquid are in contact with one another. They can't be pushed much closer together (they can't be compressed much), because they are already touching.

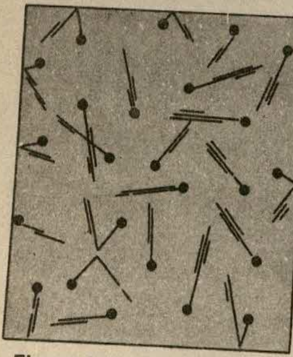


Figure 6.1 According to the kinetic-molecular theory, particles of a gas are in constant motion, occasionally bouncing off one another and the walls of their container.

The particles of a gas are in such rapid motion and are so light that gravity has little effect on them. They move up and down and sideways with ease and will not fall to the bottom of a container (as a liquid, for example, will). Any container of gas is completely filled. By *filled* we do not mean that the gas is packed tightly, but rather that it is distributed throughout the container's entire volume. A particle moves along a straight path unless it strikes something (another particle or the walls of the container). Then it may bounce off at an angle and travel from the point of collision along a straight path until it hits something else. These collisions are perfectly elastic. That simply means that there is no tendency for the collection of particles to slow down and eventually stop. Two particles that are about to collide have a certain combined kinetic energy. After the collision the sum of their kinetic energies is the same. One of the particles may have been slowed down by the collision, but the other will have been speeded up just enough to compensate (**figure 6.1**).

The kinetic-molecular theory explains what it is we are measuring when we measure temperature. According to the theory, temperature is just a reflection of the kinetic energy of the gas particles. The higher the kinetic energy, that is, the faster the particles are moving, the higher the temperature of the sample. On the average, the particles of a cold sample are moving more slowly than the particles of a hot sample. In any single sample, some particles are moving faster than others. Temperature reflects the *average* kinetic energy of the particles.

As a particle strikes a wall of its container, it gives the wall a little push. (If you were hit with a baseball or a brick, you would feel a push.) The sum of all these tiny pushes over a given area of the wall is what we call pressure. Thus, when someone says that your automobile tire pressure is 28 pounds per square inch (psi), it means that every square inch of your tire is experiencing a force of 28 lb due to the fact that billions of gas atoms are striking the tire's walls.

6.3 Atmospheric and Other Pressures

Molecules of air are constantly bouncing off each of us. Molecules are so tiny, though, that we don't feel the impact of individual ones. In fact, at ordinary altitudes we don't feel the molecules pushing on our skin, because there are molecules on the inside pushing out just as hard. When we increase our altitude rapidly by driving up a mountain or riding an elevator up to the top of a tall building, however, our ears pop because there are fewer molecules (because of the thinner air) on the outside pushing in than there

Several other units of pressure are widely used. Weather reports often include atmospheric pressure in inches of mercury.

$$1 \text{ atm} = 29.92 \text{ in. Hg} = 760 \text{ mm Hg}$$

Engineers generally use pounds (of air) per square inch (psi).

$$1 \text{ atm} = 14.7 \text{ psi}$$

Another unit of pressure, used by respiratory therapists, is centimetres of water. Such measurements assume water to be the liquid in the barometer.

$$1 \text{ cm } H_2O = 1.36 \text{ mm Hg}$$

The SI unit for pressure is the pascal (Pa), a unit that is interpreted in terms of newtons (N). (A newton is the force which, when applied to a mass of 1 kg, will give that mass an acceleration of 1 m/second during each second.)

$$1 \text{ Pa} = 1 \text{ N/m}^2$$
$$1 \text{ atm} = 101\ 325 \text{ Pa}$$

The pascal has not come into widespread use in the United States as yet.

are on the inside pushing out. Once we are at the top of the mountain or building, the pressures are soon equalized and the popping stops.

The pressure of the atmosphere is measured by a device called a *barometer*. The simplest type of barometer is a long glass tube, closed at one end, filled with mercury, and inverted in a shallow dish containing mercury (**figure 6.2**). Suppose the tube is 1 m long. Some of the mercury in the tube will drain into the dish, but *not all* of it. The mercury will drain out only until the pressure exerted by the mercury remaining in the tube exactly balances the pressure exerted by the atmosphere on the surface of the mercury in the dish. The mercury in the tube is trying to push its way out under the influence of gravity, and the air pressure is pushing it back in. At some point they reach a stalemate. Mercury is a very heavy (dense) liquid. On the average, at sea level, a column of mercury 760 mm high will balance the push of a column of air many kilometres high. The average atmospheric pressure at sea level is thus said to be 760 mm Hg. This pressure is called 1 *atmosphere* (atm) or standard pressure. The unit *millimetres of mercury* is also called a *torr* (after the Italian physicist Evangelista Torricelli, the inventor of the mercury barometer).

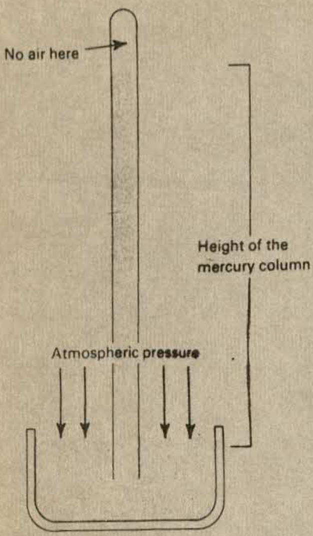


Figure 6.2 A mercury barometer.

$$760 \text{ mm Hg} = 1 \text{ atm} = 760 \text{ torrs}$$

6.4 Boyle's Law and Breathing

The relationship between the volume and the pressure of a gas was first determined by Robert Boyle in 1662. This relationship, called *Boyle's law*, states that, for a given mass of gas at constant temperature, the volume varies inversely with the pressure. When the pressure goes up, the volume goes down. When the pressure goes down, the volume goes up (**figure 6.4**). Think of gases as pictured in the kinetic-molecular theory. A sample of gas in a container exerts a certain pressure because the particles are bouncing against the walls with a certain force at a certain rate. If the volume of the container is expanded, the particles will have to traverse a longer distance before they

Figure 6.3 Robert Boyle. (Duplication courtesy of the Smithsonian Institution, Washington, D.C.)

strike the walls. Also, the surface area of the walls increases as the volume increases, so each unit of area is struck by fewer particles. Thus, the rate of these strikes (these "pushes") goes down, and the pressure measurement reflects this.

Mathematically, Boyle's law is written

$$V \propto \frac{1}{P}$$

where the symbol $\propto$ means "is proportional to." This may be changed to an equation by insertion of a *proportionality constant*, k.

$$V = \frac{k}{P}$$

Or

$$VP = k$$

This is an elegant and precise, if somewhat abstract, way of summarizing a lot of experimental data. The equation $VP = k$ says what **figure 6.4** says. If the product of V times P is to be a constant, then if V goes up P must come down. A typical Boyle's law experiment is diagrammed in **figure 6.5.** Gas is enclosed in a cylinder fitted with a movable piston. In the example, the gas occupies a volume of 1 ℓ under 1 atm of pressure. When the pressure is increased to 2 atm, the volume is reduced to 0.5 ℓ. When the pressure is 4 atm, the volume becomes 0.25 ℓ.

Boyle's law has a number of practical, as well as theoretical, applications. These are perhaps best illustrated by a number of examples. Note that in applications of Boyle's law any units for pressure or volume can be used, as long as the use is consistent.

Example 6.1 A cylinder of oxygen has a volume of 2.0 ℓ. The pressure of the gas is 1470 psi at 20 °C. What volume will the oxygen occupy at standard atmospheric pressure (14.7 psi), assuming no temperature change?

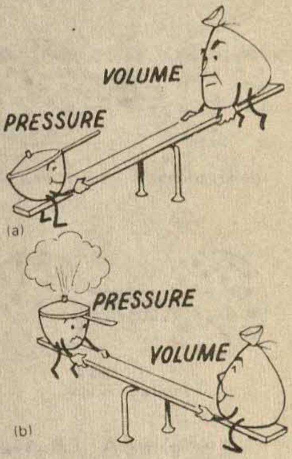


Figure 6.4 The pressure-volume relationship is like a seesaw. (a) When the pressure goes down, the volume goes up. (b) When the pressure goes up, the volume goes down. (From an idea by Cindy Hill.)

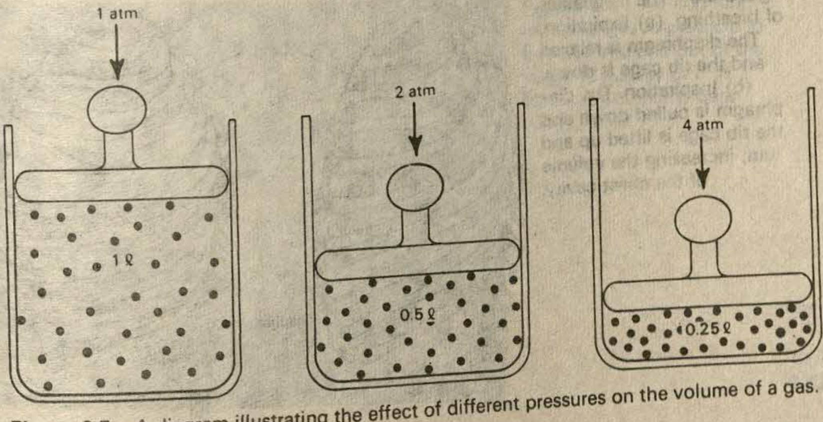


Figure 6.5 A diagram illustrating the effect of different pressures on the volume of a gas.

The simplest way to work problems of this type is to evaluate them as follows. You are asked for the volume that results when the pressure is changed from 1470 psi to 14.7 psi. The pressure has been decreased; therefore, the volume must increase. But by how much? To find out, multiply by a fraction made up of the two pressures. To make the fraction greater than 1 (so the volume will increase) arrange the pressures with the larger one on top. This way:

$$\frac{1470\ \text{psi}}{14.7\ \text{psi}}$$

and not like this:

$$\frac{14.7\ \text{psi}}{1470\ \text{psi}}$$

Then

$$2.0\,\ell \times \frac{1470\ \text{psi}}{14.7\ \text{psi}} = 200\,\ell$$

Gases are stored for use (in hospitals, for example) under high pressure, even though they will be used at atmospheric pressure. This arrangement allows much oxygen to be stored in a small area.

Example 6.2 A space capsule is equipped with a tank of air that has a volume of 0.1 m^3. The air is under a pressure of 100 atm. After a space walk, during which the cabin pressure is reduced to 0, the cabin is closed and filled with the air from the tank. What will be the final pressure if the volume of the capsule is 12.5 m^3?

Since the volume in which the air is confined increases, the pressure must decrease; therefore, the multiplier must be a fraction less than 1.

$$100\ \text{atm} \times \frac{0.1\ \text{m}^3}{12.5\ \text{m}^3} = 0.8\ \text{atm}$$

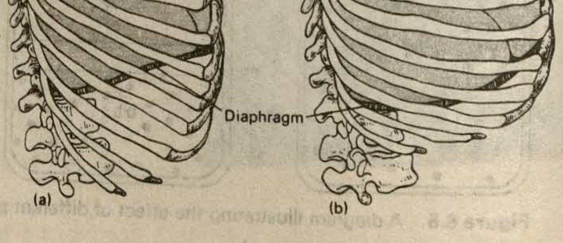


Figure 6.6 The mechanics of breathing. (a) Expiration. The diaphragm is relaxed and the rib cage is down. (b) Inspiration. The diaphragm is pulled down and the rib cage is lifted up and out, increasing the volume of the chest cavity.

Example 6.3 A weather balloon is partially filled with helium gas. On the ground, where the atmospheric pressure is 740 mm Hg, the volume of the balloon is 10 m^3. What will the volume be when the balloon reaches an altitude of 5300 m, where the pressure is 370 mm Hg?

Since the pressure decreases, the volume will increase.

$$10\ \text{m}^3 \times \frac{740\ \text{mm Hg}}{370\ \text{mm Hg}} = 20\ \text{m}^3$$

The pressure-volume relationship can be used to explain the mechanics of breathing. When we breath in (inspire), the diaphragm is lowered and the chest wall is expanded (**figure 6.6**). This increases the volume of the chest cavity. According to Boyle's law, the pressure inside the cavity must decrease. Outside air enters the lungs because it is at a higher pressure than that in the chest cavity. When we breathe out (expire), the diaphragm rises and the chest wall contracts. This decreases the volume of the chest cavity. The pressure is increased, and some of the air is forced out (**figure 6.7**).

The lungs are never emptied completely, however. The space around the lungs is maintained at a slightly lower pressure than the lungs themselves, causing the lungs to be kept partially inflated by the higher pressure within them. If a lung, the diaphragm, or the chest wall is punctured, allowing the two pressures to equalize, the lung will collapse. Sometimes a lung will be collapsed intentionally to give it time to heal. Closing the opening reinflates the lung.

People were breathing long before Boyle announced his law, but it is satisfying to understand how the process works. We get more than just satisfaction out of science, though. An understanding of the pressure-volume relationship has enabled us to keep people alive. When paralysis prevents people from being able to breathe, they can be kept alive by artificial respirators. The iron lung, which kept many polio victims alive during the 1950s, was a sealed chamber connected to a compressor and bellows (**figure 6.8**). The pressure in the chamber was varied rhythmically. When the pressure was increased, the chest cavity was compressed, and air was forced

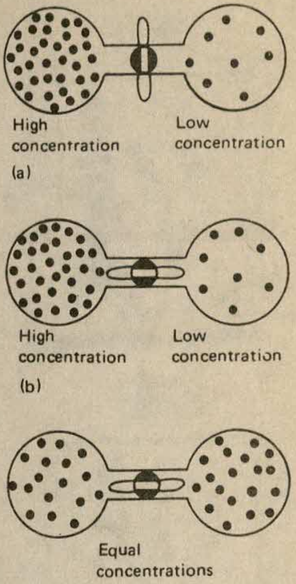


Figure 6.7 A gas (air in the lungs, for example) flows from an area of high concentration to an area of low concentration. (a) With the stopcock closed, no flow is possible. (b) With the stopcock open, there is a net flow of gases from the area of higher concentration on the left to the area of lower concentration on the right. (c) With the stopcock open, there is no net flow of gas, because concentrations are equal.

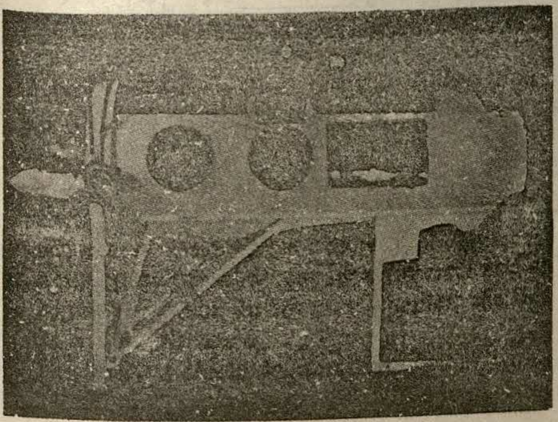


Figure 6.8 An iron lung uses changes in pressure to force air into and out of the lungs. (Courtesy of J. H. Emerson Company, Cambridge, Mass.)

out of the lungs. When the pressure was decreased, the chest expanded, and air was drawn into the lungs.

The iron lung, designed to enclose the patient completely (except for the head), was cumbersome and uncomfortable. It has been replaced by respirators that enclose the chest only. In fact, the whole area of respiratory therapy has become far more complicated in recent years. Specialists in this area are rapidly becoming an indispensable part of the medical team. In many respects, the increasing sophistication of respiratory therapy resembles the earlier development of anesthesiology.

6.5 Charles' Law: Hot Air, Big Balloon

In 1787, the French physicist J. A. C. Charles studied the relationship of the volume of a gas to the temperature, at constant pressure. Charles found that, if he took a given volume of a gas at 0 °C and cooled it, at constant pressure, to −1 °C, the volume was reduced by $\frac{1}{273}$. Let's assume that for an experiment we take 273 ml of a gas at 0 °C. If the gas is cooled to −1 °C, the volume will be decreased by $\frac{1}{273}$.

$$\frac{1}{273} \times 273\ \text{ml} = 1\ \text{ml}$$

The new volume will be 272 ml. If the gas is cooled to −10 °C, the volume will be 263 ml. A decrease of 10 °C means a decrease of $\frac{10}{273}$ in volume.

$$\frac{10}{273} \times 273\ \text{ml} = 10\ \text{ml}$$

This sort of experiment suggests that if a gas could be cooled to −273 °C it would have *zero* volume. In reality, gases liquefy before reaching −273 °C. It was from experiments of this sort, though, that the zero point for the absolute, or Kelvin, scale of temperature (section 1.5) was determined.

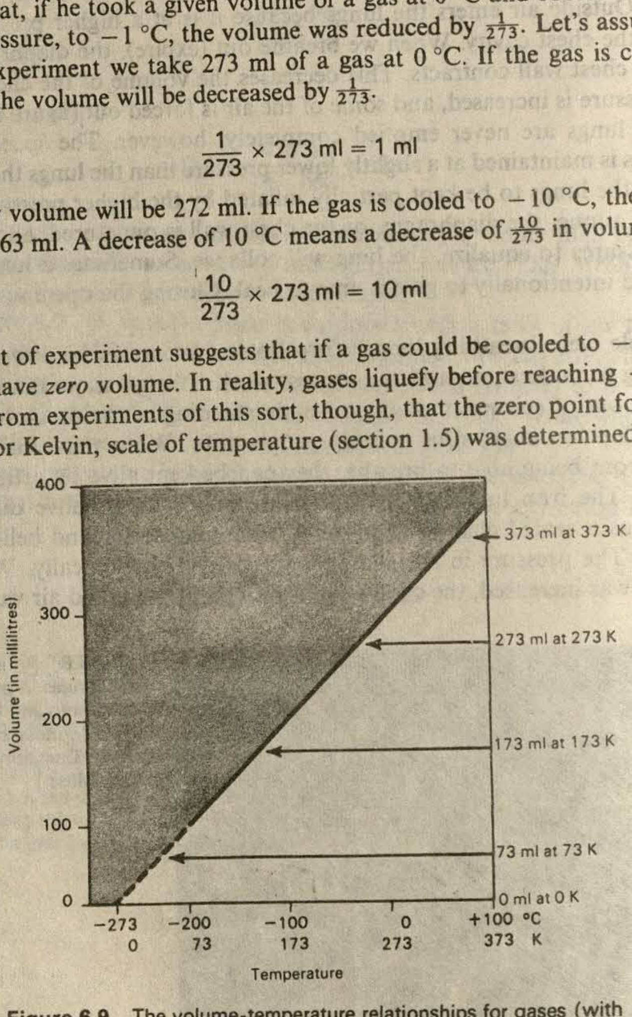


Figure 6.9 The volume-temperature relationships for gases (with pressure constant).

Charles' law states that the volume of a gas is directly proportional to its temperature (on the Kelvin scale) if the pressure is held constant. Mathematically this relationship is expressed as

$$V \propto T$$

In the form of an equation, this becomes

$$V = kT$$

or

$$\frac{V}{T} = k$$

As the temperature increases, so does the volume. Again let us emphasize that the temperature increase (or decrease) must be based on the absolute temperature scale. In the case of temperature (unlike that of volume or pressure), the units of measurement for gas law calculations are restricted.

The kinetic-molecular model accounts for this relationship. If we heat a gas, we supply it with energy, and the particles of the gas begin moving faster. These speedier particles strike the walls of their container harder and more often. If the pressure is to remain constant, the volume of the container must increase. Now, since the particles will take longer to travel from one wall to another and since the area of the walls increases when the volume increases, each unit of area will be hit less often. The pressure exerted by more slowly moving (low-temperature) particles confined within the smaller volume will be the same as the pressure of the faster-moving (high-temperature) particles contained within the larger volume.

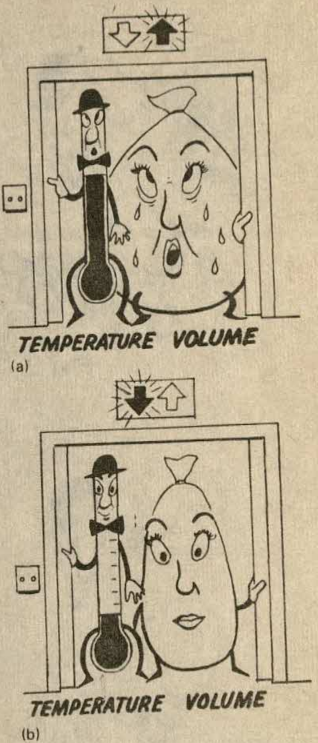


Figure 6.10 Temperature and volume are like passengers on an elevator. (a) When one goes up, the other must go up also. (b) When one goes down, the other goes down too. (From an idea by Cindy Hill.)

Example 6.4 A ballon, indoors where the temperature is 27 °C, has a volume of 2.0 ℓ. What will be its volume outside where the temperature is −23 °C? (Assume no change in pressure.)

First, convert all temperatures to the Kelvin scale. The initial temperature is

$$273 + 27 = 300 \text{ K}$$

The final temperature is

$$273 - 23 = 250 \text{ K}$$

As the temperature decreases, the volume must also decrease.

$$2.0\ \ell \times \frac{250 \text{ K}}{300 \text{ K}} = 1.7\ \ell$$

Example 6.5 What would be the final volume of the balloon in example 6.4 if it were measured where the temperature was 47 °C? (Assume no change in pressure.)

The initial temperature is

$$273 + 27 = 300 \text{ K}$$

The final temperature is

$$273 + 47 = 320\ \text{K}$$

In this case, since the temperature increases, the volume must also increase.

$$2.0\ \ell \times \frac{320\ \text{K}}{300\ \text{K}} = 2.1\ \ell$$

6.6 Gay-Lussac's Law: Hot Air, High Pressure

At about the same time that Charles was doing the experiments on which his law is based, Joseph Gay-Lussac, a French chemist, was also working with gases. His experiments showed that at constant volume pressure is directly proportional to absolute temperature. Mathematically, this is expressed as

$$P \propto T$$

In the form of an equation, this becomes

$$P = kT$$

or

$$\frac{P}{T} = k$$

As the temperature increases at constant volume, so does the pressure. At the higher temperature, the particles move faster and hit the walls of their container harder and more often, and, thus, the pressure increases.

Example 6.6 Automobile tires are filled to a pressure of 30 psi at 20 °C. The tires become hot from high-speed driving and reach a temperature of 50 °C. What will the pressure be at that temperature? (Assume that the volume remains constant.)

The initial temperature is

$$273 + 20 = 293\ \text{K}$$

The final temperature is

$$273 + 50 = 323\ \text{K}$$

The temperature increases, so the pressure must also increase.

$$30\ \text{psi} \times \frac{323\ \text{K}}{293\ \text{K}} = 33\ \text{psi}$$

Example 6.7 At 127 °C the pressure in an autoclave is 2.0 atm. What will the pressure be at 27 °C?

The initial temperature is

$$273 + 127 = 400\ \text{K}$$

The final temperature is

$$273 + 27 = 300\ \text{K}$$

The temperature decreases; therefore, the pressure must also decrease.

$$2.0\ \text{atm} \times \frac{300\ \text{K}}{400\ \text{K}} = 1.5\ \text{atm}$$

6.7 Putting It All Together: The Combined Gas Laws

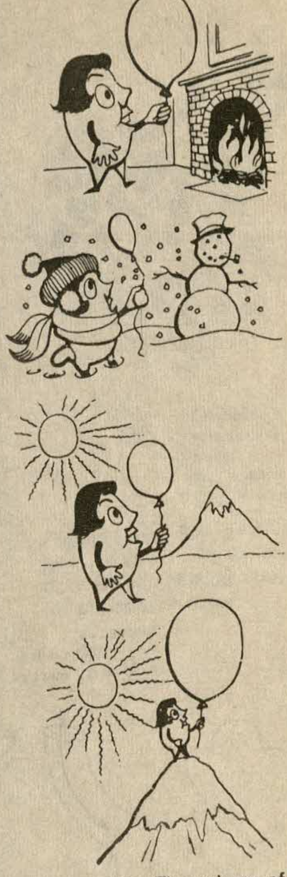


Figure 6.11 The volume of a gas varies with temperature and pressure.

We have seen that the volume of a gas varies considerably with both temperature and pressure. If we want to compare two samples, we have to do so at identical temperatures and pressures for the comparison to be meaningful. We can use Boyle's law and Charles' law, combined, to calculate the volume of a gas at any given temperature and pressure provided we know its volume at any other temperature and pressure.

Example 6.8 A balloon is partially filled with helium on the ground at 27 °C and 740 mm Hg pressure. Its volume is 10 m^3. What would the volume be at an altitude of 5300 m, where the pressure is 370 mm Hg and the temperature is −23 °C?

First, since volume is inversely related to pressure, the pressure decrease would lead to a volume increase.

$$10\ \text{m}^3 \times \frac{740\ \text{mm Hg}}{370\ \text{mm Hg}} = 20\ \text{m}^3$$

Second, since the volume is directly proportional to the absolute temperature, the temperature decrease would lead to a volume decrease. The initial temperature is

$$273 + 27 = 300\ \text{K}$$

The final temperature is

$$273 - 23 = 250\ \text{K}$$

$$20\ \text{m}^3 \times \frac{250\ \text{K}}{300\ \text{K}} = 17\ \text{m}^3$$

It does not matter in which order you do these two calculations. The final answer will be the same. It is usual to combine both changes in one equation.

$$10\ \text{m}^3 \times \frac{740\ \text{mm Hg}}{370\ \text{mm Hg}} \times \frac{250\ \text{K}}{300\ \text{K}} = 17\ \text{m}^3$$

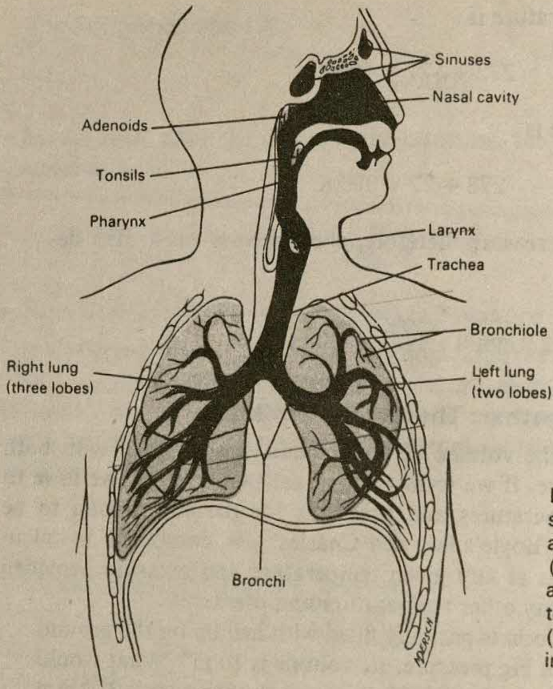


Figure 6.13 The respiratory system, showing the route of air through the nose, pharynx (throat), larynx (voice box), and trachea (windpipe), into the bronchi and bronchioles (bronchial tubes) and ending in the alveoli (air sacs).

Hyperbaric chambers were also used to treat infections by anaerobic bacteria (bacteria that live without air). Gangrene is one such disease. The organisms that cause gangrene cannot survive in an oxygenated atmosphere. If sufficient oxygen can be forced into the diseased tissues, the infection can be arrested.

6.10 Partial Pressures and Pulmonary Processes

When we breathe in, the inspired air becomes moistened and warmed to our body temperature of 37 °C. If atmospheric pressure is taken to be 760 mm Hg, the partial pressure of oxygen (P_{O_2}) is about 150 mm Hg. The partial pressure of carbon dioxide (P_{CO_2}) in inspired air is only about 0.2 mm Hg. The air in the aveoli, the tiny air sacs of the lungs at which the respiratory tract terminates (**figure 6.13**), contains oxygen and carbon dioxide at partial pressures of about 104 mm Hg and 40 mm Hg respectively. (Partial pressures are sometimes referred to as gas tensions in respiratory therapy.) Since gases flow from regions of higher concentration to regions of lower concentration, oxygen is transferred from the inspired air to the alveoli, from a region with a P_{O_2} of 150 mm Hg to a region with a P_{O_2} of 104 mm Hg. For the same reason, carbon dioxide will flow out of the alveoli to be exhaled, from a region with a P_{CO_2} of 40 mm Hg to a region with a P_{CO_2} of 0.2 mm Hg (**figure 6.14**).

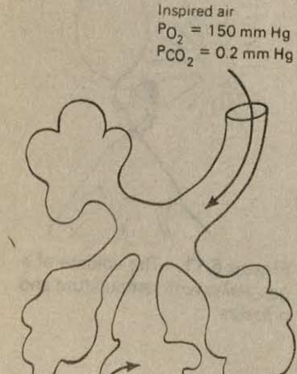


Figure 6.14 Oxygen flows from the inspired air into the alveolar air. Carbon dioxide flows in the opposite direction In each case, the flow is from a region of high partial pressure to a region of low partial pressure.

Capillaries carry venous blood past the alveoli. Gases diffuse through the thin membranes separating the capillary from the alveolar sac. The P_{O_2} in the venous blood is about 40 mm Hg. Therefore, oxygen will flow from the alveolus (where its P_{O_2} is 104 mm Hg) into the capillary. Carbon dioxide in the venous blood is at a P_{CO_2} of 46 mm Hg. Thus, carbon dioxide will flow from the capillary to the alveolus, where the P_{CO_2} is only 40 mm Hg. In this manner, venous blood is reoxygenated as it passes the alveoli (**figure 6.15**).

After the blood has passed the alveoli, its P_{O_2} has reached 100 mm Hg and its P_{CO_2} has been reduced to 40 mm Hg. This oxygen-enriched fluid is now arterial blood. When the arterial blood reaches the tissues, it passes into small arteries called arterioles. The body cells are surrounded by extracellular fluid, where the P_{O_2} is about 30 mm Hg and the P_{CO_2} is about 45 mm Hg. Thus, oxygen diffuses from the arterioles into the extracellular fluid, and carbon dioxide flows in the opposite direction (**figure 6.16**).

It is in the cell that oxygen is used in the production of energy. The cell contains oxygen at a P_{O_2} of about 6 mm Hg. Oxygen diffuses across the cell membrane from the extracellular fluid into the cell. Carbon dioxide, produced as a by-product of cell metabolism, is at a P_{CO_2} of about 50 mm Hg inside the cell. The cell therefore gives up carbon dioxide to the extracellular fluid (**figure 6.17**) and thence into the blood. This venous blood is carried back to the heart and is pumped to the lungs, where it is once again oxygenated.

Given the mechanical action of the chest and diaphragm (section 6.4) to get air into and out of the lungs, the remaining process is all downhill. It is merely a matter of gases diffusing from areas of higher pressure to areas of lower pressure.

Overall, we are constantly removing oxygen from the air and dumping our waste carbon dioxide into the atmosphere. Plants reverse the process, using carbon dioxide as fuel and dumping oxygen into the atmosphere.

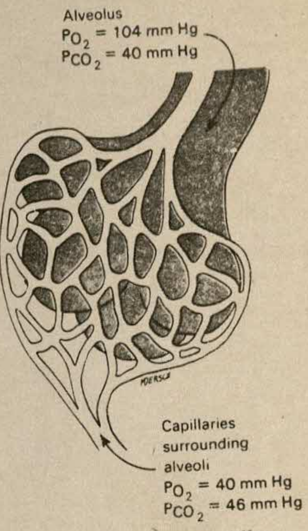


Figure 6.15 Oxygen diffuses from the alveolus to the capillary. Carbon dioxide moves in the opposite direction.

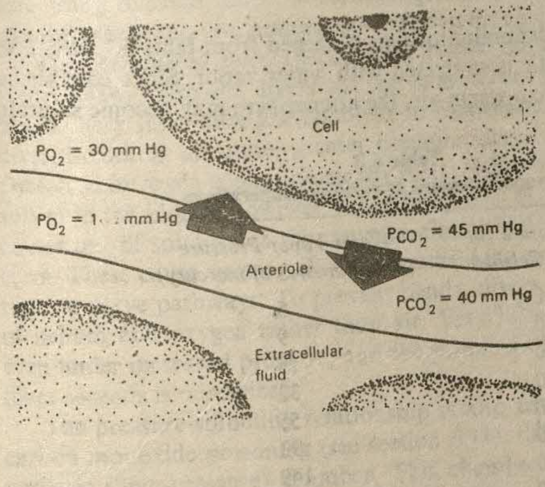


Figure 6.16 Oxygen diffuses from an arteriole into the extracellular fluid. Carbon dioxide flows in the reverse direction.

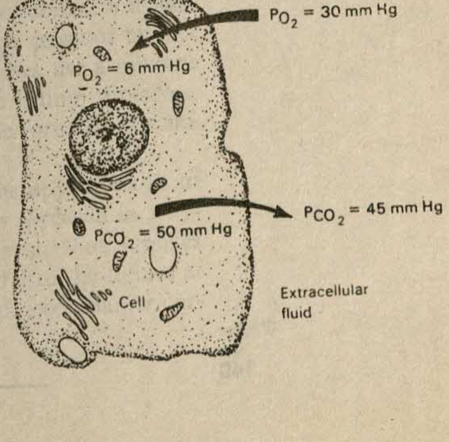


Figure 6.17 Oxygen diffuses into a cell from the extracellular fluid. Carbon dioxide moves in the opposite direction.

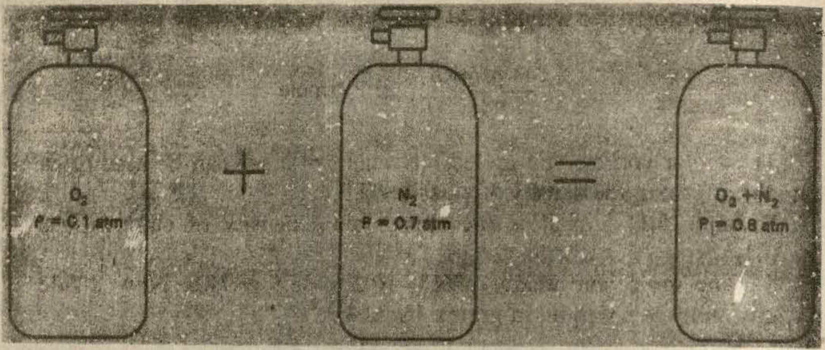


Figure 6.12 Dalton's law of partial pressures states that the pressure of a mixture of gases is equal to the sum of the pressure that each would exert by itself.

From **table 6.2** we find that the vapor pressure of water at 20 °C is 18 mm Hg. Since the total pressure is equal to 740 mm Hg, we have

$$740 \text{ mm Hg} = P_{O_2} + 18 \text{ mm Hg}$$
$$P_{O_2} = 740 - 18 = 722 \text{ mm Hg}$$

Humidity is a measure of the amount of water vapor in the air. *Relative humidity* is the ratio (expressed as a percentage) of the vapor pressure of water in the air to the vapor pressure of water in a saturated air sample at the same temperature. If the temperature is 20 °C and the vapor pressure of water in the atmosphere is 12 mm Hg, then the relative humidity is

$$\frac{12 \text{ mm Hg}}{18 \text{ mm Hg}} \times 100 = 67\%$$

The 18 mm Hg in the denominator was obtained from **table 6.2.** When the humidity is 100%, the air is saturated with water vapor. Since cool air can hold less water vapor than warm air, the atmosphere may become saturated

Table 6.2
Water vapor pressure at various temperatures

Temperature (in degrees Celsius)	*Water Vapor Pressure (in millimetres of mercury)*
0	5
10	9
20	18
30	32
40	55
50	93
60	149
70	234
80	355
90	526
100	760

as the temperature falls during the evening and early morning hours. The result is dew, water that has condensed from the air as the air became saturated.

Respiratory therapists must concern themselves with the humidity of the gases they administer to patients. Normally, as one breathes, the inspired air is saturated with moisture as it passes through the nose and respiratory passages. Oxygen as it comes from a tank is quite dry. If oxygen is being administered over a long period of time, it must be humidified to prevent it from irritating the mucous linings of the nasal passages and the lungs. If the oxygen or mixture of gases is conducted through the nose, the therapist may merely assist the normal body processes by imparting about 30% humidity to the inspired gases. If the breathing mixture is conducted directly to the trachea (bypassing the nose), the therapist saturates the gas mixture with water vapor.

6.9 Henry's Law: Soda Pop, the Bends, and Gangrene

In the 1760s Joseph Priestley invented soda water by dissolving carbon dioxide gas in water. No doubt you have noticed the hissing sound and the formation of bubbles when you opened a bottle of pop (or beer or champagne, for that matter). Carbon dioxide is dissolved in the liquid and the bottle is capped under pressure. William Henry, a close friend of John Dalton, spent a great deal of time studying the solubility of gases in liquids. In 1801 he summarized his findings in the law we know as *Henry's law*. The solubility of a gas in a liquid at a given temperature, he found, is directly proportional to the pressure of the gas at the surface of the liquid. To get back to the bottle of pop: when the bottle was capped under pressure a certain amount of carbon dioxide was dissolved in the pop. When you opened the bottle, the pressure was *reduced* (the hissing sound you heard was pressure being released) and the solubility of the carbon dioxide was *reduced* (the bubbles of gas you noticed were carbon dioxide escaping from solution).

The carbonated beverage industry is not the only group interested in Henry's law. Deep-sea divers get the bends from nitrogen dissolved in the blood. Very little nitrogen dissolves in our blood at normal pressures. A diver, breathing air under greater pressure, dissolves appreciable amounts. Dissolved nitrogen is physiologically inert: it doesn't do any harm while dissolved in the blood. However, if a diver comes up too rapidly, the nitrogen comes out of solution as the pressure diminishes. Tiny bubbles of nitrogen form. These cause severe pain in the arms, legs, and joints, perhaps by disrupting nerve pathways. To prevent bends, divers sometimes use a mixture of helium and oxygen rather than air. Very little of the helium dissolves, even under increased pressure, and the problem of bubble formation as the diver ascends is minimized.

The pressure-solubility relationship is also used in therapy. In cases of carbon monoxide poisoning (see section 6.11), the victim is placed in a hyperbaric (high-pressure) chamber. This chamber is a device that supplies oxygen at pressures of 3 or 4 atm. More oxygen is forced into the tissues at these pressures to compensate for the lack of oxygen that accompanies carbon monoxide poisoning.

Chemists have found it convenient to define *standard conditions of temperature and pressure* (referred to as STP) as 0 °C (273 K) and 1 atm (760 mm Hg).

Example 6.9 You find in a reference book that 4.0 g of helium occupy 22.4 ℓ at STP. How large a balloon could you fill with 4.0 g of helium at 22 °C and 720 mm Hg?

Since the pressure decreases, the volume must increase.

$$22.4\ \ell \times \frac{760\ \text{mm Hg}}{720\ \text{mm Hg}} = 23.6\ \ell$$

The temperature increase would also lead to a volume increase. The initial temperature is

$$273 + 0 = 273\ \text{K}$$

The final temperature is

$$273 + 22 = 295\ \text{K}$$

$$23.6\ \ell \times \frac{295\ \text{K}}{273\ \text{K}} = 25.6\ \ell$$

Or

$$22.4\ \ell \times \frac{760\ \text{mm Hg}}{720\ \text{mm Hg}} \times \frac{295\ \text{K}}{273\ \text{K}} = 25.6\ \ell$$

Densities of gases usually are reported in the literature in terms of grams per litre at STP. Recall (section 5.4) that there are 6.02×10^{23} molecules in 1 mole of any gas. Recall also that the weight of 1 mole of gas is merely the formula weight expressed in grams. Now, if we divide the molecular weight (in grams) by the density at STP (in grams per litre), we will get the volume occupied by a mole of gas at STP. For example, the density of nitrogen gas (N_2) at STP is 1.25 g/ℓ. The molecular weight of nitrogen gas is 28 g. Dividing, we get

$$\frac{28\ \text{g/mole}}{1.25\ \text{g}/\ell} = 22.4\ \ell/\text{mole}$$

For oxygen (O_2) the density at STP is 1.43 g/ℓ. The molecular weight is 32. Dividing, we get

$$\frac{32\ \text{g/mole}}{1.43\ \text{g}/\ell} = 22.4\ \ell/\text{mole}$$

In fact, the volume occupied by a mole of most gases at STP is quite close to 22.4 ℓ. This quantity is known as the *molar volume* of a gas.

Example 6.10 What is the molar volume of carbon dioxide, which has a density of 1.98 g/ℓ at STP?

The molecular weight is 44. Dividing, we get

$$\frac{44\ \text{g/mole}}{1.98\ \text{g}/\ell} = 22.2\ \ell/\text{mole}$$

The molar volume and molecular weight of a gas can be used to calculate the approximate density of a gas at STP.

Example 6.11 What is the approximate density of chlorine gas (Cl_2)?

The molecular weight of Cl_2 is $2 \times 35.5 = 71.0$. Now divide this molecular weight, in grams, by 22.4 ℓ.

$$\frac{71.0\ \text{g/mole}}{22.4\ \ell/\text{mole}} = 3.17\ \text{g}/\ell$$

The experimental value is 3.21 g/ℓ, with a difference of only 1%.

6.8 Dalton's Law of Partial Pressures: Your Gas Is All Wet

John Dalton is most renowned for his atomic theory (section 2.3). But Dalton had wide-ranging interests, including meteorology. In trying to understand the weather, he did a number of experiments on water vapor in the air. In one experiment, he found that, if he added water vapor at a certain pressure to dry air, the pressure exerted by the air would increase by an amount equal to the pressure of the water vapor. Based on this and other experiments, Dalton concluded that each of the gases in a mixture behaves independently of the other gases. Each gas exerts its own pressure. The total pressure of the mixture is equal to the sum of the *partial pressures* exerted by the separate gases (**figure 6.12**).

Mathematically, Dalton's law is stated as

$$P_{\text{total}} = P_1 + P_2 + P_3 + \cdots$$

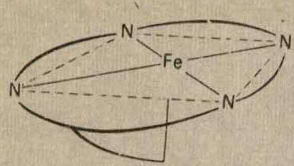
where the terms on the right side refer to the partial pressures of gases 1, 2, 3, and so on.

Gases such as oxygen, nitrogen, and hydrogen are nonpolar. They are only slightly soluble in water and are usually collected over water by the technique of displacement. Such gases always contain water molecules, and the total pressure in the collection vessel is that of the gas plus that of water vapor.

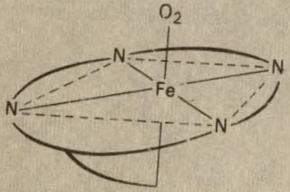
The vapor pressure of water depends upon the temperature of the water (**table 6.2**). The hotter the water, the higher the vapor pressure. We can make use of vapor pressure tables to calculate the pressure due to the gas alone by noting the temperature and subtracting the vapor pressure of water at that temperature from the total pressure within the collection vessel.

Example 6.12 Oxygen is collected over water at 20 °C. The pressure inside the jar is 740 mm Hg. What is the pressure due to oxygen alone?

$$P_{\text{total}} = P_{O_2} + P_{H_2O}$$



Hemoglobin



Oxyhemoglobin

Figure 6.18 Schematic representations of hemoglobin and oxyhemoglobin.

6.11 A Personalized Rapid Transit System: Hemoglobin

So far we have explained the movement of blood gases on the basis of pressure gradients. We also discussed the solubility of gases in terms of Henry's law. Our bodies, however, need a lot more oxygen than can be dissolved in blood plasma alone. Most of the oxygen in the bloodstream is taken up by the red blood cells. In these cells it is combined with hemoglobin, a huge, complex molecule that contains iron atoms. Schematic diagrams of hemoglobin and its oxygen complex (called oxyhemoglobin) are shown in **figure 6.18.**

The formation of oxyhemoglobin is favored by a high P_{O_2}, a relatively low temperature, and other conditions that exist in the capillaries that bound the alveoli of the lungs at inspiration. When the blood reaches the tissues, the oxyhemoglobin encounters opposite conditions, under which the oxyhemoglobin dissociates, allowing the oxygen to diffuse into the cells.

Hemoglobin also participates in the transport of carbon dioxide, but only to a slight extent. Most of the carbon dioxide is transported as bicarbonate ion (HCO_3^-) dissolved in the blood. Some is carried as the simple dissolved gas. In the lungs, the bound carbon dioxide is released. It diffuses into the alveoli and is exhaled.

It is interesting to note that, normally, the carbon dioxide level in the blood (not the oxygen level) acts as a trigger for the breathing process. To oversimplify, when carbon dioxide levels build up, we take a breath; if they get too low, we don't. Thus, one of the concerns of a therapist is the partial pressure of carbon dioxide in the blood. It is possible for the carbon dioxide level to build up so much that the heart starts beating wildly. It is also possible, under certain unusual conditions, for the level of carbon dioxide to fall so low that it fails to trigger the breathing mechanism, so that a patient with access to a plentiful supply of oxygen might simply stop breathing.

Other chemical substances also react with hemoglobin. Most notorious, perhaps, is carbon monoxide (CO). This odorless, tasteless gas is formed in large quantities when carbonaceous fuels are burned in insufficient oxygen. Millions of tons of carbon monoxide (about 80% of it from automobile exhausts) are poured into our atmosphere each year. Carbon monoxide binds so tightly to hemoglobin that the latter becomes unavailable for oxygen transport. The symptoms of carbon monoxide poisoning are, therefore, those of oxygen deprivation. Drowsiness is an early symptom, followed by impairment of physical and mental processes. Excessive amounts, as would be found in a closed garage with an automobile running, can cause death. All except the most severe cases of carbon monoxide poisoning are reversible. Treatment with pure oxygen, in a hyperbaric chamber, if possible (section 6.9), is the best antidote. Artificial respiration may help if pure oxygen is not available.

Problems

1. Define or explain the following terms.
   a. Boyle's law
   b. Charles' law
   c. Dalton's law
   d. Henry's law
   e. mm Hg
   f. psi

g. partial pressure
h. torr
i. diffusion
j. the kinetic-molecular theory

2. List the four major gases found in dry air. Which of these are important in respiration?
3. Why is atmospheric pressure greater at sea level than on the top of a high mountain?
4. Explain how a mercury barometer works.
5. A tank of oxygen contains 2.0 ft^3 of oxygen at 1470 psi. What volume will the oxygen occupy at standard atmospheric pressure (14.7 psi), assuming no temperature change?
6. A child is given a balloon which has a volume of 5.0 ℓ at standard pressure. What will be the volume of the balloon if it is taken into a hyperbaric chamber where the pressure is 4 atm?
7. Two flasks are connected. Flask A has oxygen at a P_{O_2} of 460 mm Hg. Flask B has oxygen at a P_{O_2} of 320 mm Hg and nitrogen at a P_{N_2} of 240 mm Hg. Which direction will the net flow of oxygen take? Answer the same question for nitrogen.
8. An automobile tire is inflated to 30 psi at 27 °C. What will be the pressure at 127 °C, assuming no volume change?
9. A balloon is filled with helium. Its volume is 5.0 ℓ at 27 °C. What will be its volume at -73 °C, assuming no pressure change?
10. If a gas occupies 4 ℓ at a temperature of 25 °C and a pressure of 2 atm, what volume will it occupy at a temperature of 200 °C and a pressure of 1 atm?
11. What volume will 500 ml of a gas, measured at 27 °C and 720 mm Hg, occupy at STP?
12. What is the molar volume of methane (CH_4) gas, which has a density of 0.72 g/ℓ at STP?
13. Calculate the approximate density of sulfur dioxide (SO_2) gas at STP.
14. Oxygen is collected over water. If the volume is 460 ml at 740 mm Hg and 30 °C, what would be the partial pressure of oxygen alone (P_{O_2}) under these conditions? (The vapor pressure of water at 30 °C is 32 mm Hg.)
15. If the P_{H_2O} of the air is 16 mm Hg on a day when the temperature is 30 °C, what is the relative humidity? Information provided in problem 14 will be useful.
16. Why does oxygen flow from the alveoli to the pulmonary capillaries? Why does carbon dioxide flow in the reverse direction?
17. What effect does carbon monoxide have on oxygen transport?

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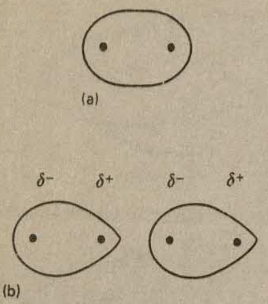

Figure 7.5 Electron cloud shapes on hydrogen molecules. (a) Average picture with no net dipole. (b) Instantaneous pictures with momentary dipoles. The transient dipoles are constantly changing, but the net result is attraction.

plain the fact that nonpolar compounds such as bromine (Br_2) and iodine (I_2) exist in the liquid and solid states? Even hydrogen can exist as a liquid or a solid if the temperature is low enough. Something must hold these molecules together.

The answer arises from the fact that the electron cloud pictures that we talked about in section 4.7 are only *average* positions. On the average, electrons spend more time near the fluorine atom in a fluorine-hydrogen bond, and this average, uneven sharing is what we have termed a dipole. On the average, the two electrons in the hydrogen molecule are between (and equidistant from) the two nuclei. The electrons are equally shared in this case. At any given instant, however, the electrons may be at one end of the molecule. At some other time, microseconds later, the electrons may be at the other end of the molecule. Such electron motions give rise to momentary dipoles (**figure 7.5**). One dipole, however momentary, can induce a similar momentary dipole in a neighboring molecule. At the instant that the electrons of one molecule are at one end, the electrons in the next molecule will move away from its adjacent end. Thus, at this instant there will be an attractive force between the electron-rich end of one molecule and the electron-poor end of the next. These transient, attractive forces (usually small) between molecules are called *dispersion forces.**

Recall that fluorine (F_2) and chlorine (Cl_2) are gases, that bromine (Br_2) is a liquid, and that iodine (I_2) is a solid. Dispersion forces are greater for larger molecules than for smaller ones. Iodine molecules are attracted to one another more strongly than bromine molecules are attracted to one another. Bromine molecules have greater dispersion forces than chlorine molecules, and chlorine molecules, in turn, have greater dispersion forces than fluorine molecules. If you look at a periodic table, you will see that this is the order in which these elements (called, as a group, the halogens) appear in Group VIIA, with iodine the largest and fluorine the smallest. Dispersion forces, to a large extent, determine the physical properties of nonpolar compounds (section 7.7).

7.5 Interionic Forces

Another type of force, already mentioned in section 4.4, is that between ions. Generally, interionic forces are the strongest of all the forces that hold solids and liquids together. In fact, nearly all ionic compounds are solids at room temperature. The energy available to most ionic compounds at room temperature is not sufficient to break the very strong forces of attraction between them. Indeed, most ionic compounds melt only at extremely high temperatures.

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*Dispersion forces are sometimes called London forces, after Fritz London, professor of chemical physics at Duke University, who first treated them systematically in 1930. They are also called van der Waals forces, in honor of the Dutch physicist, Johannes D. van der Waals. Actually, van der Waals forces include all types of attractive forces between molecules, not just dispersion forces.

Recall that ions are electrically charged. Those with opposite charges attract one another. The attraction is not usually limited to just a pair of ions. Rather, each ion is attracted by several oppositely charged ions that surround it (see **figure 4.2**). As we've said, these *ionic bonds* are very strong. Whereas the attraction between dipolar molecules results from forces between centers of partial charge, in ions the attraction is between fully charged particles, those which have completely lost or gained control of electrons.

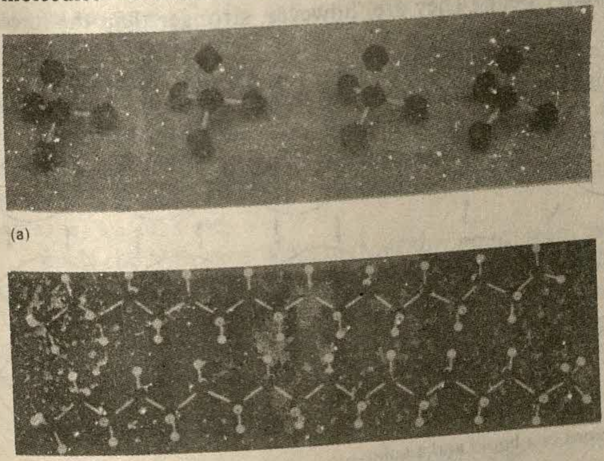
Forces are greater between ions of higher charge. The interionic force between mercury(II) ion (Hg^{2+}) and sulfide ion (S^{2-}) is greater than that between sodium ion (Na^+) and chloride ion (Cl^-). The force between aluminum ion (Al^{3+}) and nitride ion (N^{3-}) is greater still.

It should be noted that dispersion forces may be important even when other types of forces are present. Even though we might think of such forces as individually weaker than dipolar attractions or ionic bonds, in substances composed of large molecules the cumulative effect of dispersion forces may be considerable. For large ions, such as silver (Ag^+) and iodide (I^-), dispersion forces may play a significant role even though interionic forces also exist. Dispersion forces play a major role in the presence of some dipolar forces. In hydrogen chloride (HCl), for example, dipolar forces may contribute as little as 15% to the intermolecular attraction; the rest is due to dispersion forces.

7.6 The Liquid State

Molecules of a liquid are much closer together than those of a gas. Consequently, liquids can be compressed only slightly. The molecules are in constant motion, but their movements are greatly restricted by neighboring molecules. One liquid can diffuse into another, but such diffusion is much slower than in gases because of the restricted molecular motion of liquids.

The shape of the molecules which make up a liquid has an effect on one of the properties of the liquid, its *viscosity*, or resistance to flow. Liquids with low viscosity—"thin" liquids—generally consist of small, symmetrical molecules with weak intermolecular forces. Viscous liquids, on the other


(a)

(b)

Figure 7.6 (a) Carbon tetrachloride (CCl_4) consists of small, symmetrical molecules with fairly weak intermolecular forces. It has a low viscosity. (b) Octadene ($C_{18}H_{38}$) consists of long molecules with fairly strong intermolecular forces. It has a relatively high viscosity.

mined both by molecular weight (the size of the molecules) and by the type of force between molecules. If one of these two variables can be eliminated (or held constant), then simple generalizations are possible. For example, the Group VIIA elements all exist as nonpolar diatomic molecules. Intermolecular forces are similar; thus, any variation in properties can be attributed to variations in molecular weight. And we do find such a trend. Fluorine (F_2), with a molecular weight of 38, and chlorine (Cl_2), with a molecular weight of 71, are gases at room temperature. Bromine (Br_2), with a molecular weight of 160, is a liquid, and iodine (I_2), with a molecular weight of 254, is a solid. A similar trend can be found for compounds that experience similar intermolecular forces, as is the case for the following compounds of carbon and the halogens.

Compound	CF_4	CCl_4	CBr_4	CI_4
Formula weight	88	154	332	520
Physical state (at room temperature)	Gas	Liquid	Solid	Solid

The types of intermolecular force are usually of overriding importance if we are comparing molecules that are subject to dissimilar forces. We will consider the various types of force in detail in the following sections.

7.2 Dipole Forces

In section 4.8 we saw that certain unlike atoms shared electrons unequally, giving rise to polar covalent bonds. Unsymmetrical molecules containing polar bonds are themselves polar (section 4.10). Such molecules contain a center of negative charge and a center of positive charge. They are called dipoles.

Two dipoles brought close enough attract one another. The positive end of one molecule attracts the negative end of another, much as the opposite poles of a magnet attract one another. Such forces may exist throughout the structure of a liquid or a solid (**figure 7.2**). In general, attractive forces between dipoles are fairly weak. They are, however, stronger than the forces

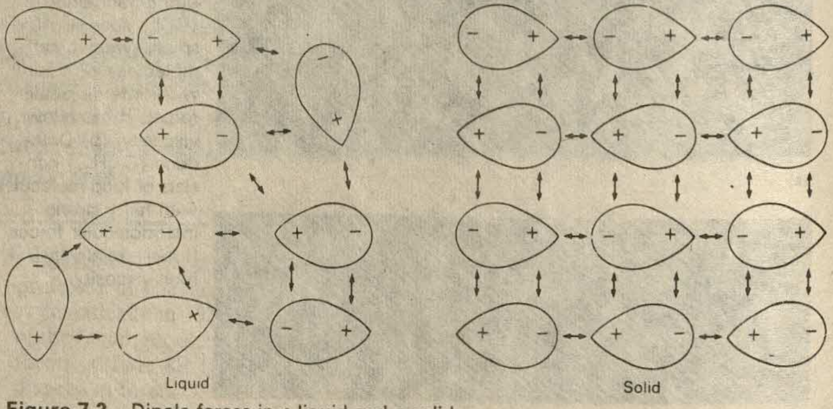


Figure 7.2 Dipole forces in a liquid and a solid.

between nonpolar molecules of comparable molecular weight. Compounds such as hydrogen chloride (HCl), hydrogen sulfide (H_2S), and sulfur dioxide (SO_2) consist of dipolar molecules.

7.3 Hydrogen Bonds

Certain molecules that have hydrogen atoms attached to fluorine, oxygen, or nitrogen have stronger attractive forces than are expected on the basis of dipolar attractive forces alone. These forces are strong enough to be given a special name, the hydrogen bond. Note that *hydrogen bond* is a somewhat misleading name since it emphasizes only the hydrogen component. Not all compounds containing hydrogen exhibit this strong attractive force. As we indicated in the first sentence of this paragraph, the hydrogen must be attached to oxygen, fluorine, or nitrogen if the molecules are to engage in hydrogen bonding. It is the presence of these atoms that permits us to offer an explanation for the extra strength of hydrogen bonds as compared to dipolar forces. Fluorine, oxygen, and nitrogen all have a high electron-attracting power (they are very electronegative). And these atoms are small, allowing the hydrogen atom on another molecule to approach closely for maximum attraction. If one pictures the bond between two atoms as an electron "cloud" (the orbital picture), then a hydrogen-fluorine bond (for example) is a much denser cloud at the fluorine end because of fluorine's power to attract electrons. This leaves the hydrogen somewhat exposed. The fluorine of another molecule can then approach the hydrogen (very closely because of the fluorine's small size) and "share" some of its wealth with the hydrogen (**figure 7.3**).

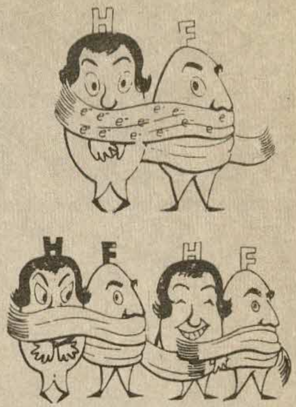
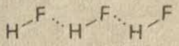


Figure 7.3 Hydrogen bonding. The electron-rich fluorine of one hydrogen fluoride molecule can share its wealth with an electron-poor hydrogen of a neighboring hydrogen fluoride molecule.

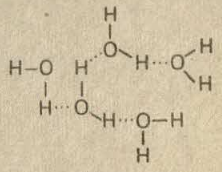
Since fluorine forms only one covalent bond, there is only one pure fluorine-containing compound, hydrogen fluoride (HF), capable of intermolecular hydrogen bonding. Oxygen-containing compounds that can form hydrogen bonds include not only water but also the alcohols (chapter 16), which are classed among the organic compounds discussed in later chapters of this book. Nitrogen-containing compounds that can form hydrogen bonds include ammonia (NH_3) and a number of organic compounds, among them the amines (chapter 19).

Hydrogen bonds are generally represented by dotted lines (**figure 7.4**). In hydrogen fluoride, the hydrogen bond is about half as strong as the hydrogen-to-fluorine covalent bond. In water, however, the hydrogen bond is only about 5% as strong as the covalent bond between hydrogen and oxygen. Nevertheless, hydrogen bonding appreciably affects the properties of water, as we shall see.

Figure 7.4 Hydrogen bonding in hydrogen fluoride and in water.



Hydrogen fluoride



Water

While the hydrogen bond may, at this point, seem merely an interesting piece of chemical theory, its importance to life and health is immense. The structure of proteins, chemicals essential to life, is determined, in part, by hydrogen bonding. And the heredity that one generation passes on to the next is encoded in genes through hydrogen bonding.

7.4 Dispersion Forces

If one understands that positive attracts negative, then it is easy enough to understand how polar molecules are held together. But how can we ex-

chapter 7

Liquids and Solids

In chapter 4 we examined the subject of bonding. Our primary concern then was how atoms combined to form molecules and why elements reacted to form compounds. Now we're going to expand our consideration of bonding, and this time we will be looking for an answer to this question: What makes a substance a solid rather than a liquid or a liquid rather than a gas? Some force of attraction holds the particles of solids and liquids in contact with one another. The particles of a gas fly about at random; those of liquids or solids cling together. Gas particles interact so little with one another that a collection of them retains neither a specific volume nor a specific shape. But particles of a liquid are held together with sufficient force that a collection of them has a specific volume. And particles of a solid are so rigidly held together that not only the volume but the shape of a given sample is fixed. Are these mysterious forces of attraction important? They are if appearances are important to you. You are built of solids and liquids. If you think you've got it all together, you should thank the special forces of attraction that give shape and volume to the condensed forms of matter.

In this chapter we're also going to consider changes in the state of matter—what happens when a solid is converted to a liquid or a liquid to a gas. Is that important? Well, consider perspiration. From the amount of advertising directed against this lowly liquid, you would think it was an unnecessary annoyance. However, were it not for the conversion of this liquid to a vapor on skin surfaces, we would find it very difficult just to survive in the temperate and tropical zones of our planet, let alone to carry out vigorous physical activity.

7.1 Sticky Molecules

Gases are easily manipulated. Changes in pressure or temperature result in volume changes that are readily measured. Not so with liquids and solids. Whereas gas particles are rather far apart, allowing gases to be considerably compressed, the particles of liquids and solids are close together. The forces between rather distant gas particles are negligible, but those between particles in the liquid or solid state may be considerable.

To illustrate the vast difference in the spacing between molecules in the gaseous and the condensed states, let's consider a given volume of water vapor (a gas) and compare it to the same volume of liquid water. At STP, 22.4 ℓ of water vapor contain 6.02×10^{23} molecules. Under the same conditions, 22.4 ℓ of liquid water would contain many times that number of molecules. We can calculate just how many. Since 1 ℓ of water weighs 1 kg, 22.4 ℓ of water weigh 22.4 kg, or 22 400 g. We know that 1 mole of water weighs 18 g and contains 6.02×10^{23} molecules (section 5.4). Therefore, we can calculate the number of molecules in 22.4 ℓ of liquid water.

$$22\,400 \text{ g} \times \frac{1 \text{ mole}}{18 \text{ g}} \times \frac{6.02 \times 10^{23} \text{ molecules}}{1 \text{ mole}} = 7490 \times 10^{23} \text{ molecules}$$

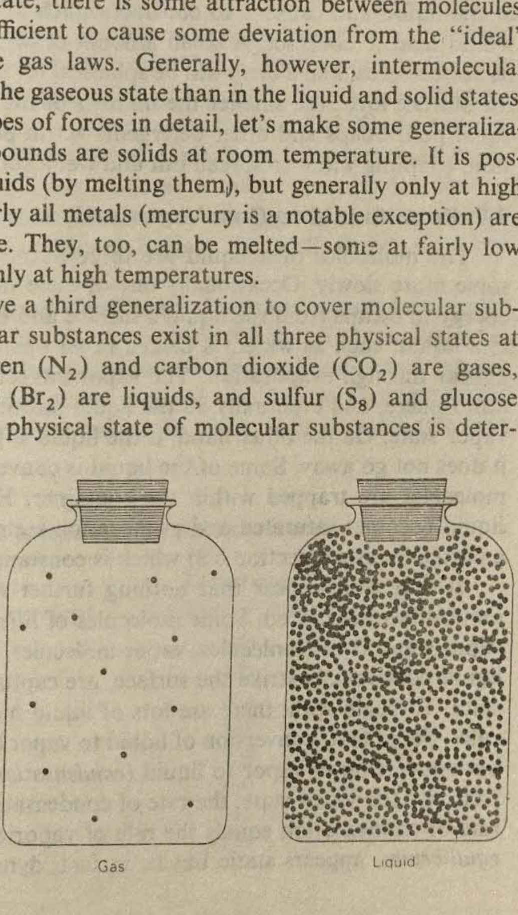
Does this mean that there are 1240 (7490/6.02) times as many molecules in the liquid as there are in the same volume of gas? Yes, and it makes for a rather crowded situation (**figure 7.1**).

Even in the gaseous state, there is some attraction between molecules. This attraction may be sufficient to cause some deviation from the "ideal" behavior described in the gas laws. Generally, however, intermolecular forces are much weaker in the gaseous state than in the liquid and solid states.

Before studying the types of forces in detail, let's make some generalizations. First, all ionic compounds are solids at room temperature. It is possible to obtain them as liquids (by melting them), but generally only at high temperatures. Second, nearly all metals (mercury is a notable exception) are solids at room temperature. They, too, can be melted—some at fairly low temperatures, but others only at high temperatures.

It would be nice to have a third generalization to cover molecular substances. However, molecular substances exist in all three physical states at room temperature. Nitrogen (N_2) and carbon dioxide (CO_2) are gases, water (H_2O) and bromine (Br_2) are liquids, and sulfur (S_8) and glucose ($C_6H_{12}O_6$) are solids. The physical state of molecular substances is deter-

Figure 7.1 There are over a thousand times as many molecules in a given volume of a liquid as there are in the same volume of a gas.



hand, are generally made up of large or unsymmetrical molecules with fairly strong intermolecular forces (such as hydrogen bonding). Viscosity generally decreases with increasing temperature. Increased kinetic energy partially overcomes the intermolecular forces. Cooking oil, for example, as it pours from the bottle is thick and, well, oily. After it's been heated in a frying pan it becomes thinner and more watery, that is, more like water in its consistency.

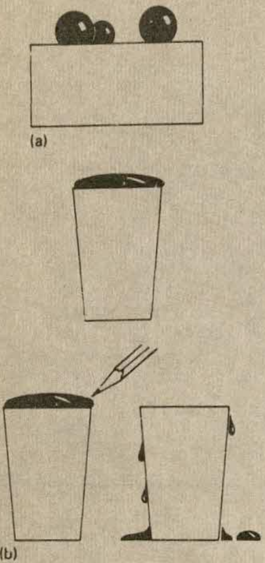
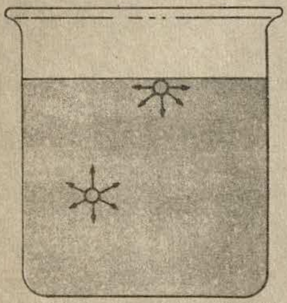


Figure 7.7 (a) Surface tension causes water droplets to form into a ball on a block of paraffin wax. (b) It also enables us to slightly "overfill" a glass.

Another property of liquids is *surface tension*. A clean glass can be slightly overfilled with water before it spills over. A small needle, carefully placed, can be made to float horizontally on the surface of water—even though steel is several times denser than water is. A variety of insects can walk or skate across the surface of a pond with ease. These phenomena indicate something quite unusual about the surface of a liquid. There is a special force or tension there that resists being disrupted by the penetration of a needle or a waterbug.

These surface forces can be explained by intermolecular forces. A molecule in the center of the liquid is pulled equally in all directions by the molecules surrounding it. A molecule on the surface, however, is attracted by molecules at its sides and below it only (**figure 7.8**). There is no corresponding upward attraction. These unequal forces tend to pull inward at the surface of the liquid and cause it to contract, much as a stretched sheet of rubber would tend to contract. A small amount of liquid will "bead" to minimize its surface area, and a drop will be spherical for the same reason. The smaller the surface area, the smaller the number of molecules experiencing the unequal pull. Soaps and other detergents act in part by lowering surface tension, enabling water to spread out and wet a solid surface.

Figure 7.8 Molecules in the body of a liquid are attracted equally in all directions. Those at the surface, however, are pulled downward and sideways, but not upward.



7.7 From Liquid to Gas: Vaporization

The molecules of a liquid are in constant motion, some moving fast, some more slowly. Occasionally one of these molecules has enough kinetic energy to escape from the liquid's surface and become a molecule of vapor. If a liquid, such as water, is placed in an open container, it will soon disappear through evaporation. The vapor molecules disperse throughout the atmosphere, and eventually all the liquid molecules escape as they enter the vapor state. On the other hand, if the liquid is placed in a closed container, it does not go away. Some of the liquid is converted to vapor, but the vapor molecules are trapped within the container. Eventually the air above the liquid becomes saturated and evaporation seems to stop. This vapor exerts a partial pressure (section 6.8) which is constant at a given temperature.

It may well appear that nothing further is happening, but molecular motion has not ceased. Some molecules of liquid are still escaping into the vapor state. Other molecules, vapor molecules, in the atmosphere above the liquid occasionally strike the surface, are captured, and return to the liquid state. To begin with, there are lots of liquid molecules and no vapor molecules. So, at first, conversion of liquid to vapor (*vaporization*) is taking place, but conversion of vapor to liquid (*condensation*) is not. As more molecules pass into the vapor state, the rate of condensation increases. Eventually, the rate of condensation equals the rate of vaporization. This condition, called *equilibrium*, appears static but is, in fact, dynamic, as we have mentioned previously. Two opposing processes are taking place at exactly the same speed. This situation is analogous to that encountered in the case of reversible chemical reactions (section 5.13).

At higher temperatures, more molecules of the liquid would have enough energy to escape from the liquid state. The vapor pressure would increase, but equilibrium would soon be reestablished at the higher temperature. The rate of vaporization would be greater, but so would the rate of condensation. At equilibrium, the rates would once again be equal (**figure 7.9**), but the equilibrium vapor pressure would be higher at the higher temperature. Schematically, these processes may be illustrated as

$$\text{Liquid} \rightleftarrows \text{vapor}$$

If a liquid is placed in an open container, the escape of molecules of the liquid is opposed by atmospheric pressure. If the liquid is heated, the vapor pressure will increase. Continued heating will eventually result in a vapor pressure equal to atmospheric pressure. At that temperature, the liquid will begin to boil. Vaporization will take place not only at the surface of the liquid but also in the body of the liquid, with vapor bubbles forming and rising to the surface. The boiling point of a liquid is the temperature at which its vapor pressure becomes equal to atmospheric pressure. Since the latter varies with altitude and weather conditions, boiling points of liquids also vary (**figure 7.10**). The cooking of foods requires that they be supplied with a certain amount of energy. When water boils at 100 °C, an egg can be placed in the water and soft-boiled to perfection in 3 minutes. If, at reduced atmospheric pressure, water boils at a lower temperature, then it contains less heat energy with which to cook the egg. It would take a bit longer to boil an egg on top of Mount Everest. Ah, well, there's no wood for a fire up there anyway.

The boiling point is increased when external pressure is increased. Autoclaves and pressure cookers are based on this principle. We can achieve a higher temperature at the higher pressures attained in these closed vessels. (Heat added to a liquid at atmospheric pressure would merely convert liquid to vapor. No increase in temperature would occur until all the liquid had

Figure 7.9 (a) Diagram of a liquid with its vapor at equilibrium in a closed container at a given temperature. Black circles represent molecules of air. (b) The same system at a higher temperature.

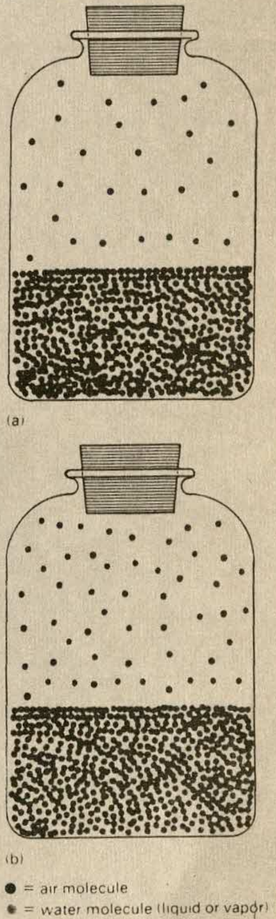


Table 7.1
Boiling points of pure water at various pressures

Pressure (in millimetres of mercury)	*Temperature (in degrees Celsius)*
760	100
816	102
875	104
938	106
1004	108
1075	110
1283	115
1535	121

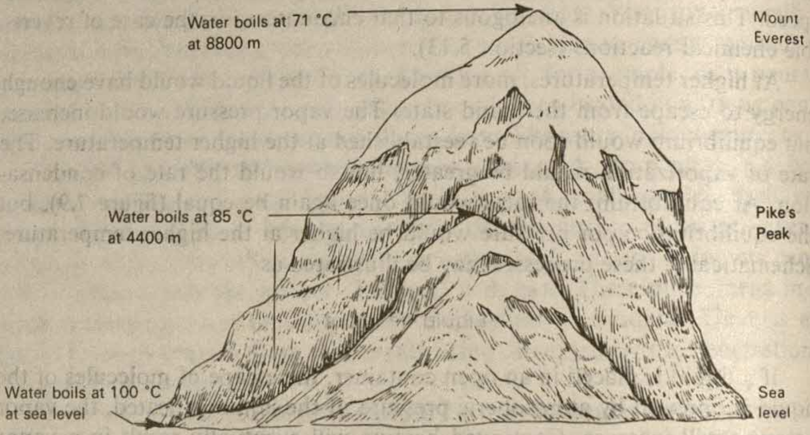


Figure 7.10 The boiling point of water at different altitudes.

vaporized.) The chemical reactions involved in the cooking of a tough piece of meat proceed more rapidly at the temperature that can be attained in a pressure cooker. Bacteria (even resistant spores) are killed more rapidly in an autoclave, not directly by the increased pressure but, rather, by the higher temperatures attained. **Table 7.1** gives the temperatures attainable with pure water at various pressures.

The boiling point of a liquid is a useful physical property, often used as an aid in identifying compounds. Since boiling point varies with pressure, it is necessary to define the *normal boiling point,* that temperature at which a liquid boils under standard pressure (1 atm, or 760 mm Hg). Alternatively, one can specify the pressure at which the boiling point was determined. For example, the *Handbook of Chemistry and Physics* (reference 12) lists the boiling point of antipyrine (a pain reliever and fever reducer) as 319^{741}. This means that the compound boils at 319 °C under a pressure of 741 mm Hg. **Table 7.2** gives the normal boiling points of some familiar liquids.

Liquids can be purified by a process called distillation. Imagine a mixture of water and some nonvolatile material, that is, some material which will not vaporize readily. If the mixture is heated until it boils, the water will vaporize, but the nonvolatile material will not. The water vapor can then

Table 7.2
Boiling points of various compounds at 1 atm

Compound	*Boiling Point (in degrees Celsius)*
Diethyl ether (anesthetic)	34.6
Methyl alcohol (wood alcohol)	64.5
Ethyl alcohol (grain alcohol)	78.3
Water	100.0
Mercury	356.6

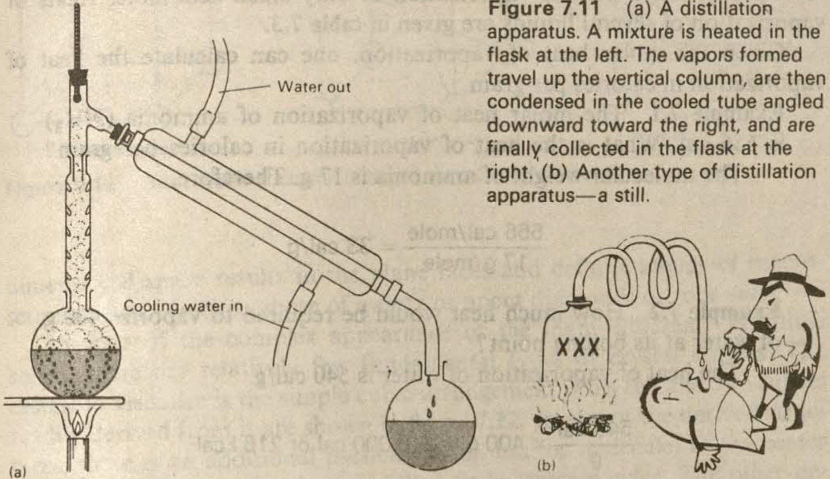


Figure 7.11 (a) A distillation apparatus. A mixture is heated in the flask at the left. The vapors formed travel up the vertical column, are then condensed in the cooled tube angled downward toward the right, and are finally collected in the flask at the right. (b) Another type of distillation apparatus—a still.

be condensed back to the liquid state and collected in a separate container. In such a distillation, the water is separated from the other component of the mixture and thereby purified.

Even if a mixture contains two or more volatile components, purification by distillation is possible. Let's consider a mixture of two components, one of which is somewhat more volatile than the other. At the boiling point of such a mixture, both components will contribute some molecules to the vapor. The more volatile component, because it is more easily vaporized, will have more of its molecules in the vapor state than will the less volatile component. When the vapor is condensed into another container, the resulting liquid will be richer in the more volatile component than was the original mixture. Thus, a purer sample of the more volatile component would have been produced.

Figure 7.11 shows a typical distillation apparatus. It is a backhanded tribute to human creativity that, spurred on by the lure of alcohol, moonshiners have been able to devise stills from the most diverse junk.

Heat is required for the conversion of a liquid to a vapor. A liquid evaporating at room temperature absorbs heat from its surroundings. Most of us are familiar with this cooling effect of evaporation. Even on a warm day, we feel cool after a swim, because the water evaporating from our skin removes heat. Volatile liquids, such as ethyl chloride (C_2H_5Cl), which boils at 12.5 °C, may be used as local anesthetics. Rapid evaporation from the skin removes enough heat to freeze a small area, rendering it insensitive to pain. Alcohol rubs also act to cool the skin by their evaporation.

The amount of heat required to vaporize a given amount of liquid can be measured. The quantity of heat required to vaporize 1 mole of a liquid at a constant pressure is called the *molar heat of vaporization*. The heat of vaporization is characteristic of a given liquid. It depends to a large extent on the type of intermolecular force in the liquid. Water, with molecules strongly associated through hydrogen bonding, has a heat of vaporization of 9.7 kcal/mole. Methane, with molecules held together by weak dispersion forces only, has a heat of vaporization of only 0.232 kcal/mole. Heats of vaporization of several liquids are given in **table 7.3.**

Given the molar heat of vaporization, one can calculate the heat of vaporization in calories per gram.

Example 7.1 The molar heat of vaporization of ammonia (NH_3) is 556 cal. What is the heat of vaporization in calories per gram?

The molecular weight of ammonia is 17 g. Therefore,

$$\frac{556 \text{ cal/mole}}{17 \text{ g/mole}} = 33 \text{ cal/g}$$

Example 7.2 How much heat would be required to vaporize 400 g of water at its boiling point?

The heat of vaporization of water is 540 cal/g.

$$\frac{540 \text{ cal}}{\text{g}} \times 400 \text{ g} = 216\,000 \text{ cal or } 216 \text{ kcal}$$

When a vapor condenses to a liquid, it gives up exactly the same amount of heat energy as was used up in converting the liquid to a vapor. A refrigerator operates by alternately vaporizing and condensing a fluid. The heat required to vaporize the fluid is drawn from the refrigerated compartment. The heat is released to the outside atmosphere when the fluid is condensed back to the liquid state.

7.8 The Solid State

Solids resemble liquids in that the particles (atoms, molecules, or ions) in them are close together, making them virtually incompressible. But these two physical states differ significantly in the motion of their molecules. In the liquid state, molecules are in constant (if somewhat restricted) motion. In solids, there is little motion other than gentle vibration about a fixed point. Consequently, diffusion in solids is generally extremely slow. An increase in temperature will increase the vigor of the vibrations in a solid. If the vibrations become violent enough, the solid will melt (section 7.9).

In many solids, the particles are arranged in regular, systematic patterns. Such solids are said to be *crystalline,* and the structure is called a *crystal lattice.* The detail of a crystal lattice can be described in terms of a small, repeating segment called a *unit cell.* Extension of these unit cells into three-

Table 7.3
Heats of vaporization (at the normal boiling point) of several liquids

Compound	*Heat of Vaporization (in calories per mole)*	*Heat of Vaporization (in calories per gram)*
Diethyl ether ($C_2H_5OC_2H_5$)	6200	84
Benzene (C_6H_6)	7300	94
Methyl alcohol (CH_3OH)	8400	260
Water	9700	540
Mercury	14 200	71

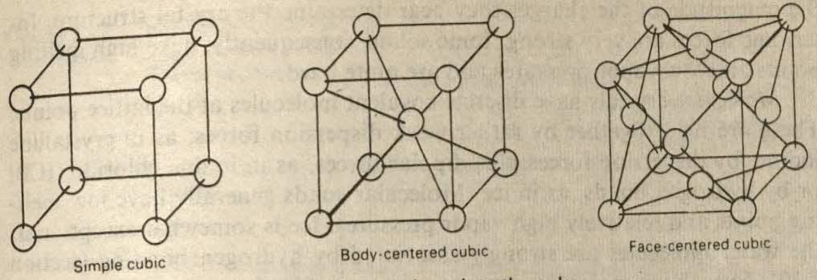


Figure 7.12 Three types of crystal lattices based on the cube.

dimensional space results in the plane faces and definite angles of macroscopic crystals (such as those of quartz or uncut diamonds or rock salt).

In spite of the complex appearance of the many different crystalline solids, there are relatively few fundamental types of crystal lattices. The easiest to visualize is the simple cubic arrangement. This cell and two others readily derived from it are shown in **figure 7.12.** In one of the derived structures, there is an additional particle (atom, ion, or molecule) at the center of the cube. This arrangement is called *body-centered cubic*. The other derived structure has particles at the center of each of the six faces of the cube. This structure is described as *face-centered cubic*. Other crystal systems are based on different geometric shapes. Two of these, the orthorhombic and hexagonal, are shown in **figure 7.13.**

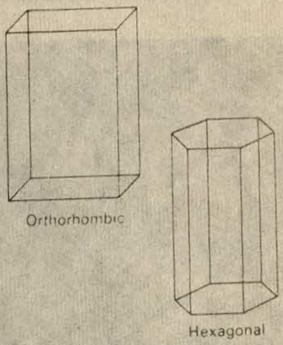
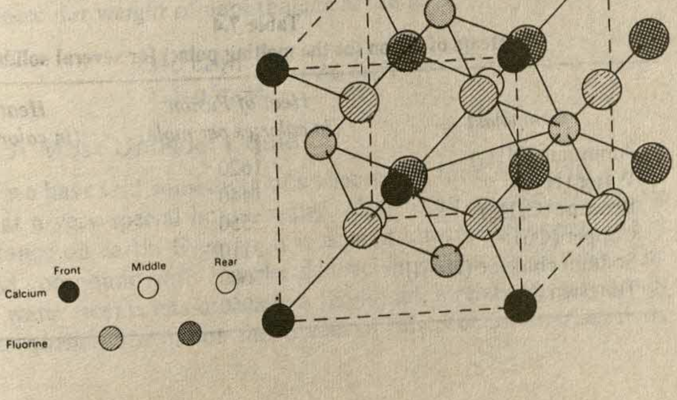


Figure 7.13 Other types of crystal lattices are based on the orthorhombic and hexagonal systems.

Crystalline solids may also be classified on the basis of the types of forces holding the particles together. The four classes are ionic, molecular, covalent network, and metallic.

Ionic solids have ions occupying the lattice points in the crystal. A typical ionic solid is sodium chloride (NaCl), which we discussed in section 4.4. In the lattice each chloride ion is surrounded by six sodium ions, and each sodium ion is surrounded by six chloride ions. In calcium fluoride (CaF_2), in which there are two fluoride ions (F^-) for each calcium ion (Ca^{2+}), the arrangement is quite different (**figure 7.14**). In calcium fluoride, each calcium ion is surrounded by only four fluoride ions. Thus, the size of the ions and

Figure 7.14 The ionic crystal lattice of calcium fluoride.



the magnitude of the charges they bear determine the crystal structure. Interionic forces are very strong. Ionic solids, consequently, have high melting points and low vapor pressures and are quite hard.

Molecular crystals have discrete covalent molecules at the lattice points. These are held together by rather weak dispersion forces, as in crystalline iodine, by dispersion forces plus dipolar forces, as in iodine chloride (ICl), or by hydrogen bonds, as in ice. Molecular solids generally have low melting points and relatively high vapor pressures. Ice is somewhat exceptional; the water molecules are strongly associated by hydrogen bonding (section 7.10). Even huge molecules, such as viruses, often have an ordered array, giving them a crystallike structure (**figure 7.15**).

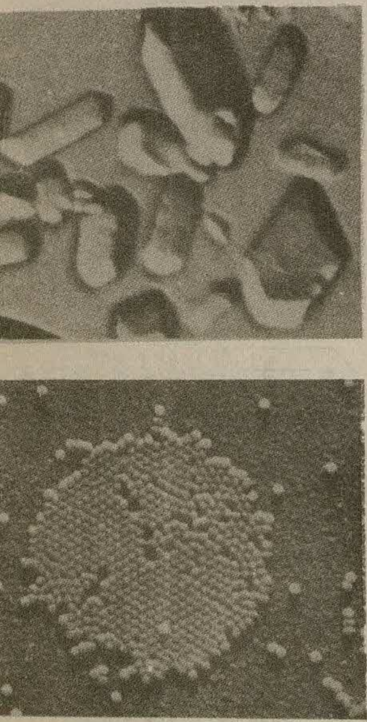


Figure 7.15 (a) Polio virus crystals, magnified 992 times. (Courtesy of F. L. Schaffer, Naval Biosciences Laboratory, Oakland, California.) (b) Spherical particles of polio virus, magnified 51 460 times. (Courtesy of the Virus Laboratory, University of California, Berkeley.)

Covalent network crystals have atoms at the lattice points. These are joined into extensive networks by covalent bonds. Thus, each crystal is in essence one large molecule. Covalent network solids are generally extremely hard and nonvolatile and melt (with decomposition) at very high temperatures. Diamond is a familiar example. Carbon atoms occupy the lattice points. Each is covalently bonded to four other carbon atoms (**figure 7.16**). Silicon carbide (SiC), also called carborundum, is another familiar compound with an extensive network of covalent bonds.

At the lattice sites in *metallic* solids are positive ions. These ions are formed when metal atoms, such as silver (Ag), lose their outer electrons. The electrons thus released are distributed throughout the lattice, almost like a fluid. These electrons, which can move freely about the lattice, make metals good conductors of heat and electricity. Some metals, such as sodium or potassium, are fairly soft and have low melting points. Others, such as manganese and iron, are hard and have high melting points. The extra electrons in iron and manganese atoms seem to lead to stronger forces between atoms. As a class, metals are malleable; that is, they can be shaped under the influence of pressure or heat. They can be rolled into bars, pressed into sheets, or extruded into wire.

7.9 From Solid to Liquid: Fusion

Most solids, when heated enough, will melt. The temperature at which this change of state occurs is called the *melting point*. The amount of heat required to convert 1 mole of a solid to a liquid at the melting point is called the *molar heat of fusion*. Generally, the heat of fusion is only a fraction of

Figure 7.16 The crystal structure of diamond, a covalent network solid.

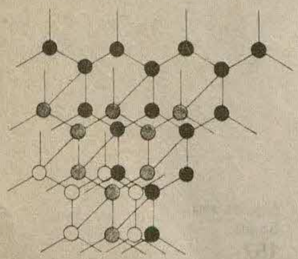
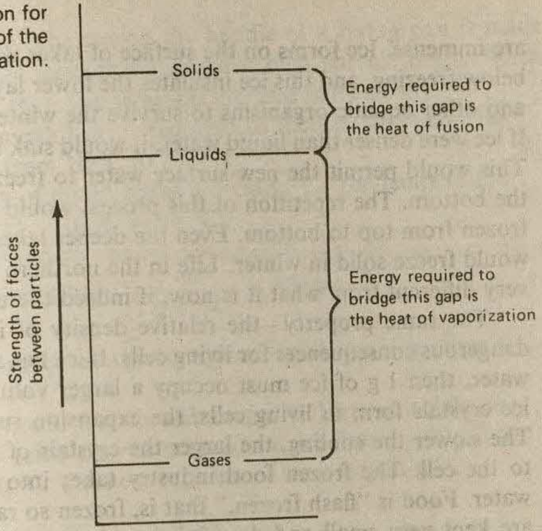


Table 7.4
Heats of fusion (at the melting point) for several solids

Compound	*Heat of Fusion (in calories per mole)*	*Heat of Fusion (in calories per gram)*
Ammonia (NH_3)	1620	95
Water (H_2O)	1440	80
Benzene (C_6H_6)	2550	33
Copper (Cu)	3110	49
Sodium chloride (NaCl)	7000	120
Tungsten (W)	8050	43

Figure 7.17 The heat of fusion for a substance is only a fraction of the heat of vaporization.


Solids
Liquids
Gases
Energy required to bridge this gap is the heat of fusion
Energy required to bridge this gap is the heat of vaporization
Strength of forces between particles

the heat of vaporization. The forces holding liquids together are not as strong as those holding solids together, but the difference between the forces holding solids together and the forces holding liquids together is much less than the difference between the forces holding liquids together and the forces holding gases together (**figure 7.17**). The heat of fusion is the amount of energy that will disrupt the crystal lattice but still leave the particles in contact with one another and under the influence of their mutual attraction. A much larger amount of energy is required to vaporize the liquid because, in vaporization, the attraction between particles must be completely overcome (or very nearly so). **Table 7.4** gives some representative heats of fusion.

Example 7.3 The heat of fusion of water is 80 cal/g. How much heat would be required to melt 400 g of ice?

$$400\text{ g} \times \frac{80\text{ cal}}{1\text{ g}} = 32\,000\text{ cal or }32\text{ kcal}$$

Example 7.4 The molar heat of fusion of naphthalene ($C_{10}H_8$) is 4610 cal. What is the heat of fusion in calories per gram?

The molecular weight of naphthalene is 128 g.

$$\frac{4610\text{ cal/mole}}{128\text{ g/mole}} = 36\text{ cal/g}$$

7.10 Water: A Most Unusual Liquid

Now that we have laid something of a theoretical foundation, let's look more closely at a very special liquid, water. Next to air, water is the most familiar substance on earth. Even so, it is a most unusual compound. It is the only liquid compound with a molecular weight as low as 18 amu. The solid form of water (ice) is less dense than the liquid, a relatively rare situation. The consequences for life on this planet of this peculiar characteristic are immense. Ice forms on the surface of lakes when the temperature drops below freezing, and this ice insulates the lower layers of water, enabling fish and other aquatic organisms to survive the winters of the temperate zones. If ice were denser than liquid water, it would sink to the bottom as it formed. This would permit the new surface water to freeze and, in its turn, sink to the bottom. The repetition of this process would eventually result in a lake frozen from top to bottom. Even the deeper lakes of the northern latitudes would freeze solid in winter. Life in the northern lakes and rivers would be very different from what it is now, if indeed there were life in those waters.

The same property—the relative density of ice and liquid water—has dangerous consequences for living cells. If ice has a lower density than liquid water, then 1 g of ice must occupy a larger volume than 1 g of water. As ice crystals form in living cells, the expansion ruptures and kills the cells. The slower the cooling, the larger the crystals of ice and the more damage to the cell. The frozen food industry takes into account this property of water. Food is "flash frozen," that is, frozen so rapidly that the ice crystals are kept very small and do minimum damage to the cellular structure of the food. The possibility of preserving human bodies for resurrection in some future age would depend on freezing the body quickly enough to prevent destruction of cells. Perhaps you have heard of plans to preserve the body of a person who dies of cancer and then to revive the body after a cure for cancer has been found. This would require freezing the body almost instantly after death. The freezing portion of the scheme has been attempted on a number of bodies. To date no revivals have succeeded.

Another unusual property of water is its high heat capacity. It takes 1 cal of heat to raise the temperature of 1 g of water 1 °C. That's 10 times as much energy as is required to raise the temperature of the same amount of iron 1 °C. The amount of energy (in calories) required to raise the temperature of 1 g of a substance 1 °C is called its *specific heat*. The specific heats of a number of common materials are given in **table 7.5**.

The reason cooking utensils are made of iron, copper, aluminum, or glass is that these materials have low heat capacities or specific heats. Thus,

Table 7.5
Specific heats of some common substances

Substance	*Specific Heat (in calories per gram per degree Celsius)*
Water (liquid)	1.0
Water (solid)	0.5
Ethyl alcohol (grain alcohol)	0.54
Wood	0.42
Glass	0.12
Iron	0.11
Aluminum	0.21
Copper	0.09
Silver	0.06
Gold	0.03

they heat up very quickly. The reason the handle of a frying pan is made of wood or plastic is that these materials have high specific heats. When they are exposed to heat, their temperatures increase more slowly.

Example 7.5 How much heat is required to increase the temperature of 10 g of water from 10 °C to 20 °C?

The heat capacity of liquid water is 1 cal/g/°C. The temperature change is 10 °C (20 °C − 10 °C = 10 °C).

$$10\text{ g} \times 10\text{ °C} \times \frac{1\text{ cal}}{(1\text{ g})(1\text{ °C})} = 100\text{ cal}$$

Example 7.6 How much energy is required to change 5 g of ice at −10 °C to steam at 100 °C?

This problem should be worked in parts. First calculate the energy required to raise the temperature of ice from −10 °C to 0 °C, a change of 10 °C. The heat capacity of ice is 0.5 cal/g/°C.

$$5\text{ g} \times 10\text{ °C} \times \frac{0.5\text{ cal}}{(1\text{ g})(1\text{ °C})} = 25\text{ cal}$$

Next, calculate, using the heat of fusion of water (80 cal/g), the energy required to melt the ice at 0 °C.

$$5\text{ g} \times \frac{80\text{ cal}}{1\text{ g}} = 400\text{ cal}$$

Then calculate the heat required to change the temperature of the water, which is at 0 °C, to 100 °C. The specific heat of water is 1 cal/g/°C, and the temperature change is 100 °C.

$$5\text{ g} \times 100\text{ °C} \times \frac{1\text{ cal}}{(1\text{ g})(1\text{ °C})} = 500\text{ cal}$$

Now calculate the amount of heat required to change the water (at 100 °C) to steam (at 100 °C). The heat of vaporization for water is 540 cal/g.

$$5\text{ g} \times \frac{540\text{ cal}}{1\text{ g}} = 2700\text{ cal}$$

Finally, total all the calculated values.

To raise the temperature of ice from −10 °C to 0 °C	25 cal
To change ice to liquid water	400 cal
To raise the temperature of water from 0 °C to 100 °C	500 cal
To change water to steam	2700 cal
Total	3625 cal

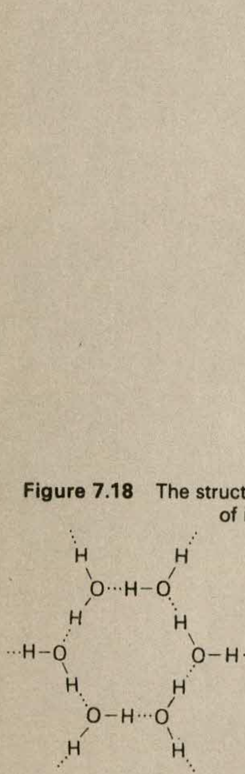
Note that almost 75% of the total energy is used in vaporizing the water.

The high heat capacity of water means not only that much energy is required to raise the temperature of water but also that much heat is given off by water for even a small drop in temperature. The vast amounts of water on the surface of the earth thus act as a giant thermostat to moderate daily temperature variations. We need only consider the extreme temperature changes on the surface of the waterless moon to appreciate this important property of water. The temperature of the moon varies from just above the boiling point of water (100 °C) to about −175 °C, a range of 275 °C. In contrast, temperatures on the earth rarely fall below −50 °C (−58 °F) or rise above 50 °C (122 °F), a range of only 100 °C.

Water also has a higher density than many other familiar liquids, including petroleum products. As a consequence, a number of liquids which are insoluble in water float on the surface of it. This situation has caused problems in recent years. Gigantic oil spills which occur when a tanker ruptures or an offshore well gets out of control result in a slick on the water's surface. This oil covers the feathers of waterfowl and the coats of sea animals, such as the otter and the seal. The oil is often washed onto beaches, where it does considerable ecological and aesthetic damage. If oil were denser than water, it would sink to the bottom. The problem would be of a different nature, though not necessarily less acute.

Still another way in which water is unusual is that it has a very high heat of vaporization; that is, a large amount of heat is required to evaporate a small amount of water. This is of enormous importance to animals. Large amounts of body heat, produced as a by-product of metabolic processes, can be dissipated by the evaporation of small amounts of water (perspiration) from the skin. The heat of vaporization of this water is obtained from the body, and the body is cooled. We previously mentioned that water's high heat capacity modifies the climate. Water's high heat of vaporization also contributes to the climate-modifying effect of lakes and oceans. A large portion of the heat that would otherwise warm up the land is used instead to vaporize water from the surface of a lake or the sea. Thus, in summer it is cooler near a large body of water than in interior land areas.

Figure 7.18 The structure of ice.



All of these fascinating properties of water result from the unique structure of the water molecule (section 4.10). Recall that the water molecule is polar. In the liquid state water molecules are strongly associated by hydrogen bonding (see **figure 7.4**). These strong attractive forces account for the high heat of vaporization of water. They must be overcome if vaporization is to take place, and this is why a large amount of energy must be supplied to water for it to convert from liquid to vapor.

In the liquid state, water molecules are quite close together but randomly arranged. In the solid state, water molecules are in a much more ordered arrangement. But this orderly arrangement, as illustrated in **figure 7.18**, is less compact than that achieved in the liquid state. Large hexagonal holes are incorporated into the ice lattice. It is this empty space that makes ice less dense than liquid water.

Because of its polar nature, water tends to dissolve ionic substances. Now, ionic solids are held together by strong ionic bonds. We have already indicated that, to melt ionic solids and break these bonds, very high temperatures are required. Yet, simply by placing sodium chloride, an ionic solid, in water at room temperature we can dissolve the salt (or, rather, the water can). And when such a solid dissolves, its bonds are broken. The difference between the two processes is the difference between brute force and persuasion. In the melting process, we are simply pouring in enough energy (as heat) to pull the crystal lattice apart. In the dissolving process, we offer the ions an attractive alternative to the crystal lattice. It works this way. Water molecules surround the lattice. As they approach a negative ion, they align themselves so that their positive ends point toward the ion. With a positive ion the process is reversed, and the negative end of the water dipole points toward the ion. Still, the attraction between a dipole and an ion is not as strong as that between two ions, so, to compensate for their weaker attractive power, the water molecules gang up on the ions. Several molecules surround each ion, and in this way the many ion-dipole interactions overcome the single ion-ion interaction. Suppose you wished to take your little sister's favorite doll from her hands. You could just pull it away, at the cost of much kicking and screaming. Or you could offer her a chance to play with your brand new pocket calculator with the pretty lights. In the latter case, she would not only give up the doll but would also regard you as her benefactor.

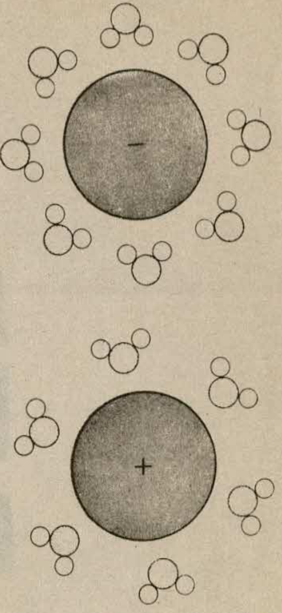
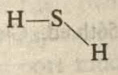


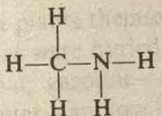
Figure 7.19 The interaction of polar water molecules with ions.

Chemical reactions in living cells take place in water solutions. Our bodies are about 65% water. The importance of solutions is such that we shall soon devote an entire chapter to the subject.

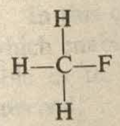
Problems

1. How do liquids and solids differ from gases in their compressibility, spacing of molecules, and intermolecular forces?
2. In what ways are liquids and solids similar? In what ways are they different?
3. List the four types of intermolecular forces. Give an example of each.
4. Describe the effect of temperature on the viscosity of a liquid.
5. Describe, in terms of intermolecular forces, the cause of the phenomenon of surface tension.
6. In which of the following compounds would hydrogen bonding be an important intermolecular force?

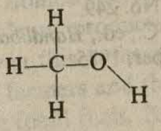
a. 

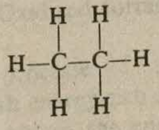
b. 

$\mathrm{H{-}\overset{H}{\underset{H}{C}}{-}\underset{H}{N}{-}H}$

c. 

$\mathrm{H{-}\overset{H}{\underset{H}{C}}{-}F}$

d. 

e. 

$\mathrm{H{-}\overset{H}{\underset{H}{C}}{-}\overset{H}{\underset{H}{C}}{-}H}$

7. How does a pressure cooker work?
8. The heat of vaporization of bromine (Br_2) is 45 cal/g. What is the *molar* heat of vaporization of bromine?
9. How is the heat of vaporization of a liquid related to intermolecular forces in the liquid?

10. The heat of fusion of water is 80 cal/g. How much heat would be required to melt a 15-kg block of ice?
11. There is a rule of thumb that says that for many liquids the molar heat of vaporization is approximately 21 times the normal boiling point in degrees Kelvin. Use this rule to calculate the molar heat of vaporization for benzene, which has a boiling point of 353 K. How does your calculated value compare to the experimental value given in **table 7.3**?
12. The specific heat of silver is 0.06 cal/g/°C. That of gold is 0.03 cal/g/°C. Which metal will be hotter (i.e., will be at a higher temperature) if both are exposed to the same amount of heat?
13. Calculate the amount of heat required to raise the temperature of 25 g of water from 20 °C to 60 °C. The specific heat of water is 1 cal/g/°C.
14. How much energy will be expended in changing 100 g of ice at −5 °C to steam at 100 °C?
15. List three distinctive properties of water.
16. Explain why a salt dissolves in water.

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chapter 8

Oxidation and Reduction

Life is a battle between two competing chemical processes called oxidation and reduction. We are losing the battle—nothing lives forever. The decay of plants, the energy-supplying reactions that permit us to grow older, and the ultimate corruption of our bodies all involve oxidation. We are, nonetheless, sustaining a magnificent delaying action. Green plants, during their lifetimes, keep us in the battle by reversing oxidation, that is, by carrying out reduction reactions in which carbon dioxide and water are ultimately converted to sugars. The process is called photosynthesis, and it requires the energy supplied by sunlight.

We attempt to maximize the efficiency of this reduction reaction. Farmers use their own muscular energy, that of domesticated animals, and the stored energy of fossil fuels (coal and petroleum products) to grow plants that support much of life on earth. Yet even this assistance depends ultimately on plants themselves—those that feed farmers and their livestock and those that were buried eons ago to form the fossil fuels. Reduced forms—sugars, coal, gasoline—are high in energy. Oxidized forms—carbon dioxide and water—are low in energy.

In this chapter we will study the processes of oxidation and reduction, which enable plants to provide us with energy-rich substances and also enable us to use those substances to obtain the energy necessary for our survival.

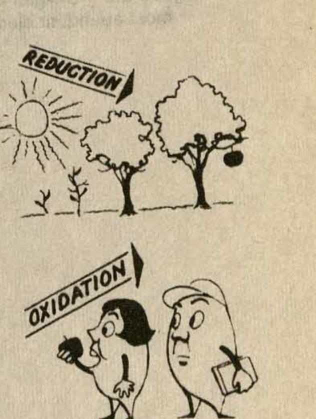

Figure 8.1 Oxidation and reduction are essential to life.

8.1 Oxygen: Abundant and Essential

It would be inaccurate to say that any one element is the most important, for there are 20 or so elements essential to life. Nevertheless, in any list of important elements, oxygen would be at or near the top. It is the most abundant of all the elements on this planet, making up about one-half the earth's crust. Oxygen occurs in each of the three subdivisions of the crust—the atmosphere, the hydrosphere, and the lithosphere. It occurs in the atmosphere (the gaseous mass surrounding the earth) as molecular oxygen (O_2). In the hydrosphere (oceans, seas, rivers, and lakes of the earth), oxygen occurs combined with hydrogen in that remarkable compound, water (H_2O). In the lithosphere (the solid portion of the earth), oxygen occurs combined with silicon (pure sand is largely SiO_2) and with a variety of metals.

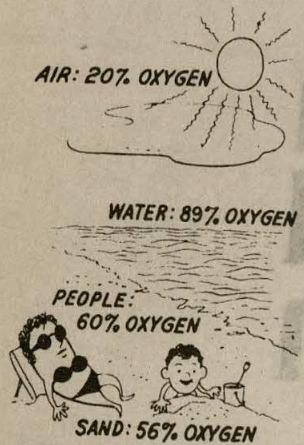

Figure 8.2 Oxygen is the most abundant element.

Oxygen is found in most of the compounds that are important to living organisms. Foodstuffs—starches, fats, and proteins—all contain oxygen. The human body is approximately 68% (by weight) water. Since 88% of the weight of water is due to oxygen, about 60% of the weight of each of us is oxygen.

Oxygen accounts for about 20% (by volume) of the atmosphere. (The other 80% is nitrogen, which enters into relatively few chemical reactions.) This oxygen, as O_2, is said to be free or uncombined, that is, not part of a compound containing another element. We have seen (chapter 6) that oxygen (in air) is taken into the lungs. From there it passes into the bloodstream. The blood carries oxygen to the body tissues, and the food we eat combines with this oxygen. This chemical process provides us with energy in the form of heat to maintain our body temperature. It also gives us the energy we need for mental and physical activity.

Oxygen performs many other functions. Fuels such as natural gas, gasoline, and coal need oxygen in order to burn and release their stored energy. Not all that oxygen does is immediately desirable, however. Oxygen causes iron to rust and copper to corrode, and it aids in the decay of wood. All these—and many other—chemical processes are called *oxidative* reactions.

8.2 Chemical Properties of Oxygen: Oxidation

When iron rusts, it combines with oxygen from the atmosphere to form a reddish brown powder.

$$4\,Fe + 3\,O_2 \longrightarrow 2\,Fe_2O_3$$

The chemical name for iron rust (Fe_2O_3) is iron(III) oxide. Many other metals react with oxygen to form *oxides*.

Most nonmetals also react with oxygen to form oxides. For example, carbon reacts to form carbon dioxide.

$$C + O_2 \longrightarrow CO_2$$

Sulfur combines with oxygen to form sulfur dioxide.

$$S + O_2 \longrightarrow SO_2$$

At high temperatures, such as those that occur in automobile engines, even nitrogen, an element which is ordinarily quite unreactive, combines with oxygen.

$$N_2 + O_2 \longrightarrow 2\,NO$$

The product, which probably should be called nitrogen monoxide, is better known as nitric oxide.*

Oxygen also reacts with many compounds. Methane, the principal ingredient of natural gas, burns in air to produce carbon dioxide and water.

$$CH_4 + 2\,O_2 \rightarrow CO_2 + 2\,H_2O$$

Hydrogen sulfide, a gaseous compound with a rotten egg odor, burns, producing water and sulfur dioxide.

$$2\,H_2S + 3\,O_2 \rightarrow 2\,H_2O + 2\,SO_2$$

In each example, oxygen combines with each of the elements in the compound.

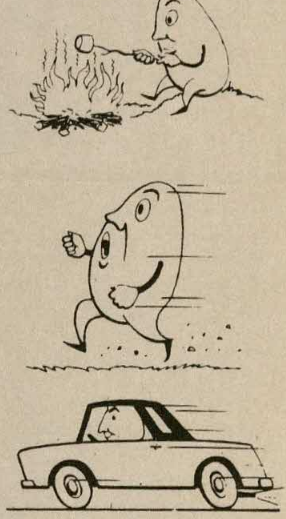

Figure 8.3 Cooking, breathing, and burning fuel all involve oxidation.

The combination of elements and compounds with oxygen is called *oxidation*. The substances which combine with oxygen are said to be *oxidized*. Originally, the term *oxidation* was restricted to reactions involving combination with oxygen. Chemists came to recognize, though, that combination with chlorine (or bromine, or other elements in the upper right portion of the periodic chart) was not all that different from reaction with oxygen. So they broadened the definition of oxidation. Oxidation is now defined in terms of *oxidation numbers*.

8.3 The (Oxidation) Numbers Game

Oxidation numbers are related to the electron density about an atom, but the relationship is not always a simple one. We will concern ourselves only with the rather arbitrary way in which these numbers are derived and with their use in studying chemical reactions involving oxidation.

If you want to play the game, you've got to learn the rules. And we'll play by the following rules in assigning oxidation numbers.

1. Free (uncombined) elements have an oxidation number of 0. Thus, oxygen, whether it occurs in the atomic form (O), in the form of a diatomic molecule (O_2), or as ozone (O_3), has an oxidation number of 0.
2. In compounds, elements in Group IA have oxidation numbers of +1 and elements in Group IIA have oxidation numbers of +2. For example, each sodium in sodium chromate (Na_2CrO_4) has an oxidation number of +1. By the same rule, calcium in calcium sulfate ($CaSO_4$) has an oxidation number of +2. In other words, the oxidation number is the same as the charge on the ion: Na^+ has +1 and Ca^{2+} has +2.
3. Hydrogen in compounds has an oxidation number of +1 except when combined with metals, in which case it is −1. In sulfuric acid (H_2SO_4), the hydrogen has an oxidation number of +1. In lithium aluminum hydride ($LiAlH_4$), since it is combined with the metals lithium and aluminum, hydrogen has an oxidation number of −1.

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*Many nonmetal oxides are named according to the number of oxygen atoms in the molecule. The Greek prefixes *mono-*, *di-*, *tri-*, and *tetra-* indicate, respectively, one, two, three, and four oxygen atoms.

4. In most compounds, oxygen has an oxidation number of −2. Thus, oxygen in sulfuric acid or sodium chromate or water has an oxidation number of −2. In special compounds called *peroxides*, oxygen's oxidation number is −1. Examples are hydrogen peroxide (H_2O_2) and barium peroxide (BaO_2). Using the formula alone, it is not always easy to distinguish a peroxide from other oxygen-containing compounds. For example, BaO_2 is a peroxide, but CO_2 is not. And CH_2O_3 may or may not be a peroxide (there are two different compounds with this formula). How will you know which is which? If we are dealing with a peroxide, we will make note of the fact, although hydrogen peroxide (H_2O_2) should be recognized by its formula. In structural formulas, peroxides are identified by the presence of an oxygen-to-oxygen bond (O—O).
5. For compounds, the algebraic sum of all the oxidation numbers must be 0. For example, in the compound sodium hydroxide (NaOH), the sodium is +1, the oxygen is −2, and the hydrogen is +1. The sum is 0.

$$(+1) + (-2) + (+1) = 0$$

6. For complex ions, the algebraic sum of all the oxidation numbers must be equal to the charge on the ion. For example, in the hydroxide ion (OH^-), the oxygen is −2 and the hydrogen is +1. The sum is −1.

$$(-2) + (+1) = -1$$

These rules are used to calculate the oxidation states of other elements in compounds. Rules 2, 3, and 4 are used first. Then rule 5 or 6 is used to calculate the oxidation number of any remaining element. You can best learn the process by working examples.

Example 8.1 What is the oxidation number of sulfur in SO_2?

Oxygen is −2 (rule 4). There are two oxygens, for a total of −4. Since the sum must be 0 (rule 5), the sulfur must be +4.

Example 8.2 What is the oxidation number of sulfur in H_2SO_4?

Hydrogen is +1 (rule 3) and oxygen is −2 (rule 4). There are two hydrogens, for a total of +2, and four oxygens, for a total of −8. Since the sum must be 0 (rule 5), we can write

$$2(+1) + 4(-2) + x = 0$$

where x is the unknown oxidation state of sulfur. Solving the equation we get

$$(+2) + (-8) + x = 0$$
$$-6 + x = 0$$
$$x = +6$$

You need not use algebra if you can see (without it) that sulfur must be +6.

Example 8.3 What is the oxidation number of nitrogen in the nitrate ion (NO_3^-)?

Oxygen is −2 (rule 4). There are three oxygen atoms, for a total of −6. Since the sum of oxidation numbers must be −1 (rule 6), we can write

$$(-6) + x = -1$$
$$x = +5$$

The nitrogen must be +5.

Example 8.4 What is the oxidation number of nitrogen in the ammonium ion (NH_4^+)?

Hydrogen is +1 (rule 3). There are four hydrogen atoms, for a total of +4. Since the sum of oxidation numbers must be +1 (rule 6), we can write

$$(+4) + x = +1$$
$$x = -3$$

The nitrogen would have to be −3.

Example 8.5 What is the oxidation number of carbon in C_2H_4O?

Hydrogen is +1. Four hydrogen atoms total +4. One oxygen is −2. Since the sum must be 0,

$$(+4) + (-2) + x = 0$$
$$x = -2$$

To balance the oxidation numbers, we need −2, so the carbons total −2. But there are two carbons to share the burden, so each carbon has an oxidation number of −1.

We now have a way to define oxidation: it is an increase in oxidation number. We can use this definition to determine whether or not oxidation has occurred in a chemical reaction. Consider the reaction

$$CaO + CO_2 \rightarrow CaCO_3$$

Is carbon oxidized? In carbon dioxide there are two oxygen atoms (each with an oxidation number of −2), for a total of −4. The carbon in carbon dioxide must be +4. Now we calculate the oxidation number of carbon in calcium carbonate ($CaCO_3$). Calcium is +2 (rule 2). Each oxygen is −2, and there are three oxygens, for a total of −6. The carbon, therefore, must be +4.

$$(+2) + (-6) + x = 0$$
$$x = +4$$

No, carbon is not oxidized in this reaction. Its oxidation number has not changed. Now consider the reaction

$$2\ Na_2CO_3 + Cr_2O_3 + 3\ KNO_3 \rightarrow 2\ CO_2 + 2\ Na_2CrO_4 + 3\ KNO_2$$

Is chromium (Cr) oxidized? The oxidation number of chromium in chromium(III) oxide (Cr_2O_3) is +3; in sodium chromate (Na_2CrO_4) it is +6. The oxidation number of chromium has increased. Therefore, it is oxidized in the reaction. Check this answer by calculating the oxidation numbers of chromium in chromium(III) oxide and in sodium chromate for yourself.

There are alternative ways (actually special cases of the oxidation number method) of defining oxidation. Three working definitions of possible utility are the following.

1. An element or compound is oxidized if it gains oxygen atoms. In the reactions encountered so far in this section, iron, carbon, sulfur, nitrogen, methane, and hydrogen sulfide all gain oxygen atoms. We say, then, that each of these substances is oxidized.
2. A compound is oxidized if it loses hydrogen atoms. Methyl alcohol, when passed over hot copper gauze, forms formaldehyde and hydrogen gas.

$$\underset{\textit{Methyl alcohol}}{CH_3OH^*} \longrightarrow \underset{\textit{Formaldehyde}}{CH_2O} + H_2$$

   Since methyl alcohol loses hydrogen atoms, it is said to be oxidized.
3. An element is oxidized if it loses electrons. When magnesium metal reacts with chlorine, magnesium ions and chloride ions are formed.

$$Mg + Cl_2 \longrightarrow Mg^{2+} + 2\ Cl^-$$

   Since the magnesium atom obviously loses electrons, it is oxidized.

We will encounter many reactions that fit these definitions when we get to the section of this book that deals with biochemistry, for it is by oxidation of foodstuffs that organisms derive their life-sustaining energy.

Why so many different definitions of oxidation? Simply for convenience. Which do we use? Whichever is most convenient. For the reaction

$$C + O_2 \longrightarrow CO_2$$

we could assign oxidation numbers and determine that carbon is oxidized (it goes from 0 to +4), but it is more convenient to see that carbon is oxidized because it gains oxygen atoms. Similarly, for the reaction

$$CH_3OH \longrightarrow CH_2O + H_2$$

we could assign oxidation numbers and determine that carbon is oxidized (it goes from −2 to 0, an *increase* of 2), but it is easier to see that carbon is oxidized because it loses hydrogen atoms. For the reaction involving chromium (p. 169), though, it would perhaps be best to calculate oxidation numbers.

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*You may have noticed that this formula is different from others we have written. Instead of CH_4O, we wrote CH_3OH. When we discuss organic compounds in later chapters, our reason for emphasizing the OH group will become clear.

8.4 Hydrogen: Lots, but Light

For every oxidation process, there is a complementary process called reduction. Before discussing reduction in detail, let's look at some of the chemistry of another important element—hydrogen.

By weight, hydrogen makes up only about 0.9% of the earth's crust, placing it far down on the list of abundant elements.* Because hydrogen is the lightest of all elements, however, hydrogen atoms are quite abundant. If we consider a random sample of 10 000 atoms from the earth's crust, 5330 are oxygen atoms, 1590 are silicon atoms, and 1510 are hydrogen atoms. Unlike oxygen, hydrogen is seldom found free in nature on earth. Most of it is combined with oxygen in water. Nearly all compounds derived from living organisms contain hydrogen. Fats, starches, sugars, and proteins all contain combined hydrogen. Petroleum and natural gas are mixtures composed mainly of hydrocarbons, compounds of hydrogen and carbon.

Since elemental hydrogen does not occur in nature (again, we limit our view to this planet), it is necessary to make it. Small amounts are made for laboratory use by the reaction of zinc with hydrochloric acid,

$$\underset{\textit{Hydrochloric acid}}{Zn + 2\,HCl} \longrightarrow \underset{\textit{Zinc chloride}}{ZnCl_2} + H_2$$

or by the reaction of calcium metal with water,

$$Ca + 2\,H_2O \longrightarrow \underset{\textit{Calcium hydroxide}}{Ca(OH)_2} + H_2$$

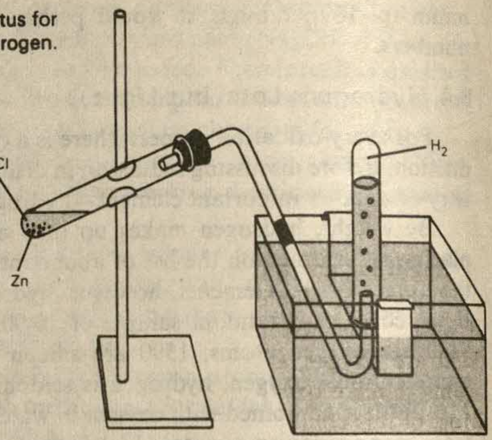
The gaseous hydrogen is easily collected by displacement of water (**figure 8.4**).

Commercially, hydrogen is usually obtained as a by-product of other processes. Much of it comes from the cracking of petroleum, a process by which oils with high boiling points are converted to fuels with lower boiling points, such as gasoline (chapter 14).

Physically, hydrogen is a colorless and odorless gas. It is essentially insoluble in water. Hydrogen is the least dense of all substances: its density is only one-fourteenth that of air under comparable conditions. For this reason it was at one time used in zeppelins (blimps) to give them the necessary

*Hydrogen ranks low in abundance on *earth*. If we look beyond our home planet, however, hydrogen becomes much more significant. The sun, for example, is largely hydrogen. In fact, hydrogen is by far the most abundant element in the universe.

Figure 8.4 A diagram of an apparatus for the laboratory synthesis of hydrogen.



buoyancy in air. However, since a spark or flame can trigger the explosion of hydrogen (section 8.5), the use of this gas represented a considerable danger. When a disastrous explosion occurred aboard a luxury airship called the Hindenburg in 1937, the use of hydrogen was discontinued, and so indeed was the commercial use of lighter-than-air ships. Those blimps still in use employ the nonreactive gas helium, while hot-air balloons use, as their name indicates, hot air, which is less dense than the atmosphere (recall Charles' law, from section 6.5).

Certain metals, such as platinum (Pt), palladium (Pd), and nickel (Ni), are capable of absorbing large volumes of hydrogen on their surface. This absorbed hydrogen appears to be a great deal more reactive than ordinary molecular hydrogen; thus, these metals are often used as catalysts for reactions involving hydrogen gas as one of the reactants.

8.5 The Chemical Properties of Hydrogen: Reduction

Chemically, a jet of hydrogen, when ignited, burns in air with an almost colorless flame. Hydrogen and oxygen may be mixed at room temperature with no perceptible reaction. However, if the mixture is ignited by a spark or flame, a tremendous explosion results. The product in both cases is water.

$$2\ H_2 + O_2 \xrightarrow{\text{spark}} 2\ H_2O$$

It is interesting to note that if a piece of platinum gauze is inserted into a container of hydrogen and oxygen, the two gases react at room temperature. The platinum acts as a catalyst: it lowers the activation energy for the reaction. The platinum will glow from the heat evolved in the initial reaction and then ignite the mixture, causing an explosion.

Hydrogen reacts with a variety of metal oxides to remove oxygen and give the free metal. For example, when hydrogen is passed over heated copper(II) oxide, metallic copper and water are formed.

$$CuO + H_2 \rightarrow Cu + H_2O$$

With lead(II) oxide, the products are metallic lead and water.

$$PbO + H_2 \longrightarrow Pb + H_2O$$

This process, in which a compound is changed, or *reduced*, to an element, is called *reduction*.

Like *oxidation*, which once simply meant combination with oxygen, the term *reduction* has been broadened in meaning. Most generally, *reduction* is defined as a *decrease* in oxidation number. In the examples above, copper goes from +2 in copper(II) oxide to 0 in metallic copper, and lead goes from +2 in lead(II) oxide to 0 in metallic lead. We say that copper and lead are reduced.

We may also use working definitions complementary to those given for oxidation (p. 170).

1. A compound is reduced if it loses oxygen atoms. In the examples above, copper(II) oxide and lead(II) oxide obviously are reduced, since they lose oxygen. When potassium chlorate ($KClO_3$) is heated, it forms potassium chloride and oxygen gas.

   $$2\ KClO_3 \xrightarrow{heat} 2\ KCl + 3\ O_2$$

   The potassium chlorate loses oxygen; therefore, it is reduced.
2. A compound is reduced if it gains hydrogen atoms. For example, methyl alcohol is produced when carbon monoxide is allowed to react with hydrogen.

   $$CO + 2\ H_2 \xrightarrow{catalyst} CH_3OH$$

   The carbon monoxide gains hydrogen; therefore, it is reduced.
3. An atom or ion is reduced if it gains electrons. When an electric current is passed through a solution containing copper(II) ions (Cu^{2+}), copper metal is plated out at the cathode.

   $$Cu^{2+} + 2\ e^- \longrightarrow Cu$$

   The copper obviously gains electrons; therefore, it is reduced.

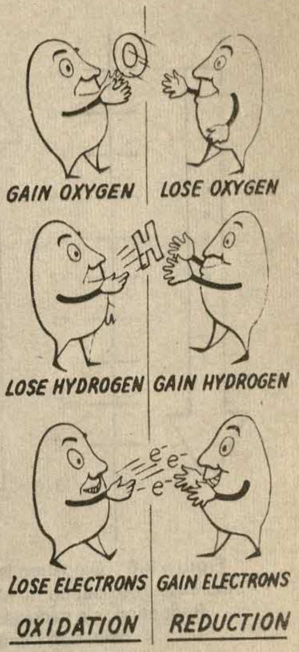


Figure 8.5 Oxidation and reduction can be defined in a variety of ways.

Oxidation and reduction go hand in hand. You can't have one without the other. When one substance is oxidized, another is reduced. For example, in the reaction

$$CuO + H_2 \longrightarrow Cu + H_2O$$

copper is reduced (from +2 to 0) and hydrogen is oxidized (from 0 to +1). Further, if one substance is being oxidized, the other must be causing it to be oxidized. In the example, copper(II) oxide is causing hydrogen gas to be oxidized. Therefore, copper(II) oxide is called the *oxidizing agent*. Conversely, hydrogen gas is causing copper(II) oxide to be reduced, so hydrogen gas is the *reducing agent*. Each oxidation-reduction (sometimes called "redox") reaction will have an oxidizing agent and a reducing agent among the reactants. The *reducing agent* is the substance being *oxidized*, and the *oxidizing agent* is the substance being *reduced*.

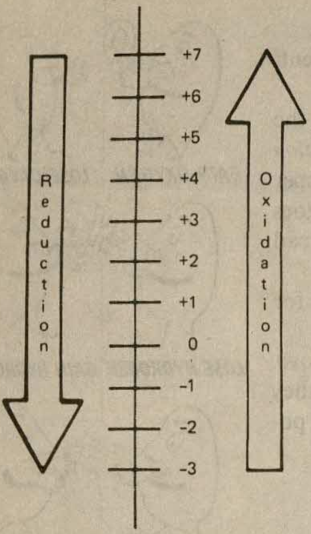


Figure 8.6 Oxidation is an increase in oxidation number. Reduction is a decrease in oxidation number.

Reduction:
copper is being reduced;
CuO is the oxidizing agent

$$\overset{+2}{\mathrm{CuO}} + \underset{0}{\mathrm{H_2}} \longrightarrow \overset{0}{\mathrm{Cu}} + \underset{+1}{\mathrm{H_2O}}$$

Oxidation:
hydrogen is being oxidized;
H_2 is the reducing agent

Example 8.6 Circle the oxidizing agent and underline the reducing agent in the following reactions.

$$\mathrm{C + O_2 \longrightarrow CO_2}$$
$$\mathrm{N_2 + 3\,H_2 \longrightarrow 2\,NH_3}$$
$$\mathrm{SnO + H_2 \longrightarrow Sn + H_2O}$$
$$\mathrm{NO + O_3 \longrightarrow NO_2 + O_2}$$
$$\mathrm{Mg + Cl_2 \longrightarrow Mg^{2+} + 2\,Cl^-}$$

The answers can be determined by means of any of the definitions previously listed.

$$\underline{\mathrm{C}} + \boxed{\mathrm{O_2}}$$

C gains oxygen and is oxidized (definition 1, section 8.3), so it must be the reducing agent. Therefore, O_2 is the oxidizing agent.

$$\boxed{\mathrm{N_2}} + 3\,\underline{\mathrm{H_2}}$$

N_2 gains hydrogen and is reduced (definition 2, section 8.5), so it must be the oxidizing agent. Therefore, H_2 is the reducing agent.

$$\boxed{\mathrm{SnO}} + \underline{\mathrm{H_2}}$$

SnO loses oxygen and is reduced (definition 1, section 8.5), so it is the oxidizing agent. H_2 is the reducing agent.

$$\underline{\mathrm{NO}} + \boxed{\mathrm{O_3}}$$

NO gains oxygen and is oxidized (definition 1, section 8.3), so it is the reducing agent. O_3 is the oxidizing agent.

$$\underline{\mathrm{Mg}} + \enclose{circle}{\mathrm{Cl}_2}$$

Mg loses electrons and is oxidized (definition 3, section 8.3), so it is the reducing agent. Cl_2 is the oxidizing agent.

8.6 Some Friendly Neighborhood Oxidizing Agents

Oxygen is undoubtedly the most common oxidizing agent. It oxidizes the wood in our campfires and the gasoline in our automobile engines. It rusts and corrodes the metals that we get by reducing ores. It even "burns" the foods we eat to give us energy to move about. It is involved in the rotting of wood and the weathering of rocks. Indeed, we live in an oxidizing atmosphere. Fortunately, though, oxygen is a mild oxidizing agent. It takes us about 70 years to "burn out."

Oxygen is sometimes used as a laboratory and industrial oxidizing agent. For example, acetylene (for cutting and welding torches) is made by the partial oxidation of methane.

$$\underset{\textit{Methane}}{4\,\mathrm{CH_4}} + 3\,\mathrm{O_2} \longrightarrow \underset{\textit{Acetylene}}{2\,\mathrm{C_2H_2}} + 6\,\mathrm{H_2O}$$

(Complete oxidation of methane would give carbon dioxide and water.) Often, though, it is more convenient to use other oxidizing agents. Potassium permanganate ($KMnO_4$) and sodium dichromate ($Na_2Cr_2O_7$) are frequently used.

Potassium permanganate is a black, shiny, crystalline solid. It dissolves in water to give deep purple solutions. This purple color disappears as the permanganate is reduced (remember, if permanganate is an oxidizing agent, it must be reduced). So potassium permanganate is often used as a test for oxidizable substances. For example, potassium permanganate is used to oxidize iron from Fe^{2+} to Fe^{3+}. The amount of iron in a sample can be determined by its reaction with permanganate. One can add permanganate solution, which is deep purple, to a sample of iron. As the permanganate is reduced, it is changed to manganese(II) ion, and the purple color disappears. When all the iron has been oxidized, the addition of more permanganate will not be accompanied by the loss of the purple color because there will be no iron(II) ion left to reduce the permanganate. Thus, one can measure just how much iron(II) ion there was in the sample by keeping track of how much permanganate was reduced, that is, by measuring how much permanganate was added until the purple color remained. The equation for this reaction is quite complex.

$$\underset{\substack{\textit{Permanganate}\\\textit{ion (purple)}}}{\mathrm{MnO_4^-}} + 9\,\mathrm{Fe^{2+}} + 8\,\mathrm{H^+} \longrightarrow \underset{\substack{\textit{Manganese(II)}\\\textit{ion (colorless)}}}{\mathrm{Mn^{2-}}} + 9\,\mathrm{Fe^{3+}} + 4\,\mathrm{H_2O}$$

Permanganate solutions can also be used to oxidize oxalic acid (a poisonous compound found in rhubarb leaves), sulfur dioxide (SO_2), and many other compounds.

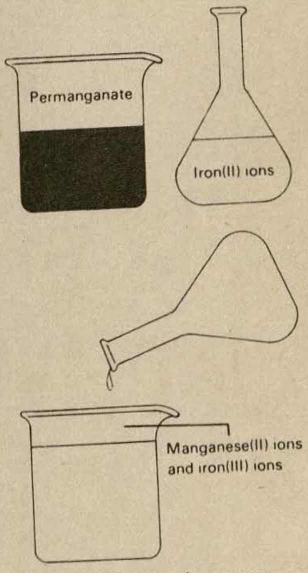


Figure 8.7 Purple permanganate ions (MnO_4^-) are reduced to Mn^{2+} by iron(II) ions (Fe^{2+}). The purple color disappears as the reaction proceeds.

Sodium dichromate is used to oxidize alcohols (chapter 16) to compounds called aldehydes and ketones. For the oxidation of ethyl alcohol (found in alcoholic beverages) to acetaldehyde, the reaction is

$$8\ H^+ + \underset{\substack{\textit{Dichromate ion} \\ \textit{(orange-red)}}}{Cr_2O_7^{2-}} + 3\ C_2H_5OH \longrightarrow \underset{\substack{\textit{Chromium(III) ion} \\ \textit{(green)}}}{2\ Cr^{3+}} + 3\ C_2H_4O + 7\ H_2O$$

Some of the tests for intoxication (the "breathalyzer," used to check for drunken drivers, for instance) depend on the oxidation of alcohol by an oxidizing agent that changes color as it is reduced (such as chromium).

Example 8.7 Calculate the oxidation number of manganese in MnO_4^- and of chromium in $Cr_2O_7^{2-}$. What are the oxidizing agents in the reactions shown on pages 175 and 176? What are the reducing agents?

Mn is reduced;
MnO_4^- is the oxidizing agent

$$\overset{+7}{MnO_4^-} + 9\ \underset{+2}{Fe^{2+}} + 8\ H^+ \longrightarrow \overset{+2}{Mn^{2+}} + 9\ \underset{+3}{Fe^{3+}} + 4\ H_2O$$

Fe is oxidized;
Fe^{2+} is the reducing agent

Cr is reduced;
$Cr_2O_7^{2-}$ is the oxidizing agent

$$8\ H^+ + \overset{+6}{Cr_2O_7^{2-}} + 3\ \underset{-2}{C_2H_5OH} \longrightarrow 2\ \overset{+3}{Cr^{3+}} + 3\ \underset{-1}{C_2H_4O} + 7\ H_2O$$

C is oxidized;
C_2H_5OH is the reducing agent

Another common oxidizing agent is hydrogen peroxide (H_2O_2). Pure hydrogen peroxide is a syrupy, colorless liquid. It is usually used as an aqueous solution, though, with concentrations of 30% and 3% generally available. Some interesting uses of hydrogen peroxide will be discussed in sections 8.8 and 8.9. For now, let's look at some of its simpler chemistry.

Hydrogen peroxide will oxidize sulfides (S^{2-}) to sulfates (SO_4^{2-}). When lead-based paints are exposed to polluted air containing hydrogen sulfide (H_2S), they turn black due to the formation of lead sulfide (PbS). Hydrogen peroxide will oxidize the black sulfide to the white sulfate.

$$\underset{\textit{(Black)}}{PbS} + 4\ H_2O_2 \longrightarrow \underset{\textit{(White)}}{PbSO_4} + 4\ H_2O$$

A nice advantage of hydrogen peroxide as an oxidizing agent is that, in most reactions, it is converted to water, an innocuous by-product.

The oxidation number of oxygen in hydrogen peroxide is −1. (Hydrogen is +1 and there are two hydrogens, so each oxygen must be −1.) When hydrogen peroxide acts as an oxidizing agent, it is reduced. The oxygen goes from −1 to −2.

Another oxidizing agent is nitric acid (HNO_3). For example, metallic copper will dissolve in nitric acid solutions because it is oxidized to copper(II) ions (Cu^{2+}).

$$Cu + 4\ HNO_3 \longrightarrow Cu(NO_3)_2 + 2\ NO_2 + 2\ H_2O$$

Example 8.8 Is HNO_3 oxidized, reduced, or neither in the reaction above?

There are four molecules of HNO_3 involved in the reaction. Two end up in $Cu(NO_3)_2$, and two end up as NO_2.

$$Cu(NO_3)_2 \longrightarrow Cu^{2+} + 2\ NO_3^-$$

No change
in oxidation
state

$$\overset{+5}{HNO_3} \longrightarrow \overset{+5}{NO_3^-}$$

HNO_3 is reduced

$$\overset{+5}{HNO_3} \longrightarrow \overset{+4}{NO_2}$$

Two of the HNO_3 molecules are reduced, but two are neither oxidized nor reduced.

Other common oxidizing agents are the halogens—fluorine (F_2), chlorine (Cl_2), bromine (Br_2), and iodine (I_2). Chlorine, for example, oxidizes magnesium metal to magnesium ions.

$$Mg + Cl_2 \longrightarrow Mg^{2+} + 2\ Cl^-$$

In the process, the oxidation number of chlorine is reduced from 0 (in Cl_2) to −1 (in Cl^-).

We will encounter some other interesting oxidizing agents in other sections.

8.7 Some Reducing Agents of Interest

There is no single reducing agent that stands out as oxygen does among oxidizing agents. Hydrogen will reduce many compounds, but it is relatively expensive for large-scale processes. Elemental carbon, or coke (obtained by driving off the volatile matter from coal), is frequently used to get metals from their ores. For example, tin can be obtained from tin(IV) oxide by reduction, with carbon used as the reducing agent.

$$SnO_2 + C \longrightarrow Sn + CO_2$$

Hydrogen may be used for the production of expensive metals such as tungsten (W). The ore is first converted to an oxide (WO_3) and then is reduced in a stream of hydrogen gas at 1200 °C.

$$WO_3 + 3\ H_2 \longrightarrow W + 3\ H_2O$$

Perhaps a more familiar reducing agent, by use if not by name, is the developer used in photography. Photographic film is coated with a silver salt (Ag^+Br^-), in which silver occurs in the +1 oxidation state. Silver ions that have been exposed to light react with the developer, a reducing agent such as the organic compound hydroquinone, to form metallic silver.

$$\underset{\textit{Hydroquinone}}{C_6H_4(OH)_2} + 2\ Ag^+ \longrightarrow C_6H_4O_2 + \underset{\textit{Silver metal}}{2\ Ag} + 2\ H^+$$

Those silver ions that were not exposed to light are not reduced by the developer. The film is then treated with "hypo," a solution of sodium thiosulfate ($Na_2S_2O_3$), which washes out unexposed silver bromide. That leaves the negative dark where the metallic silver has been deposited (where it was originally exposed to light) and transparent where light did not strike it. Light shone through the negative onto light-sensitive paper then makes the positive print.

Hydrogen peroxide, mentioned in the last section as a common oxidizing agent, is also a reducing agent. In the presence of a stronger oxidizing agent, such as permanganate, hydrogen peroxide accepts the role of reducing agent and is oxidized.

$$6\ H^+ + 2\ MnO_4^- + 5\ H_2O_2 \longrightarrow 5\ O_2 + 2\ Mn^{2+} + 8\ H_2O$$

Note that in this reaction the oxidation number of oxygen goes from −1 (in H_2O_2) to 0 (in O_2). When acting as an oxidizing agent, oxygen in hydrogen peroxide goes from −1 to −2 (in H_2O). Such behavior is characteristic of compounds with elements in intermediate oxidation states. They may go up or down the scale (be oxidized or reduced). Putting it another way, they may act as either reducing or oxidizing agents.

8.8 Oxidation and Antiseptics

Many common antiseptics (compounds that are applied to living tissue to kill or prevent the growth of microorganisms) are mild oxidizing agents. Hydrogen peroxide, in the form of a 3% aqueous solution, finds use in medicine as a topical antiseptic. It can be used to treat minor cuts and abrasions on certain parts of the body. Potassium permanganate, in concentrations ranging from 0.01% to 0.2%, can be used as a topical antiseptic and an astringent. Potassium chlorate ($KClO_3$) was once used as an antiseptic for skin and mucous membranes. Its use has been largely discontinued because it is rather irritating, somewhat toxic, and only marginally effective.

Sodium hypochlorite (NaOCl), available in aqueous solution as a laundry bleach (*Purex*, *Clorox*, and the like), finds some use in the irrigation of wounds and for bladder infections. It is also used as a disinfectant, deodorizer, and bleach (section 8.9). Solutions of iodine are frequently used as antiseptics.

The exact method of operation of these oxidizing agents as antiseptics is unknown. Their action is rather indiscriminate; they attack human cells as well as microorganisms. For many purposes, these simple inorganic compounds have been replaced by organic compounds such as the phenols (chapter 16). The simplest of the phenols (carbolic acid) has itself been replaced by less poisonous modifications of its basic structure.

Other oxidizing agents are used as disinfectants. Calcium hypochlorite [$Ca(OCl)_2$], called bleaching powder, is used to disinfect clothing and bedding. Chlorine (Cl_2) is used to kill pathogenic (disease-causing) microorganisms in drinking water. Waste water is usually treated with chlorine also, before it is returned to a stream or lake. Such treatment has been quite effective in preventing the spread of infectious diseases such as typhoid fever. Use of chlorine in this manner came under criticism in 1974, when it was shown that the chlorine reacted with organic compounds (presumably from industrial wastes) to form toxic chlorinated compounds.

Ozone has also been used to disinfect drinking water. Many European cities, including Paris and Moscow, use ozone to treat their drinking water. Ozone is more expensive than chlorine, but less of it is needed. An added advantage is that ozone kills viruses on which chlorine has little, if any, effect. Tests in Russia have shown ozone to be a hundred times as effective as chlorine for killing polio virus.

Ozone (O_3) acts by transferring its "extra" oxygen to the contaminant. The oxidized contaminants are thought to be less toxic than the chlorinated ones. In addition, ozone imparts no "chemical taste" to the water. We may well see a shift from chlorine to ozone in the treatment of our drinking water and waste water.

8.9 Oxidation: Bleaching and Stain Removal

Bleaches are compounds that are used to remove unwanted color from white fabrics. Nearly any oxidizing agent will do the job. However, some also harm the fabric, some are unsafe, some produce undesirable by-products, and some are simply too expensive.

The most familiar laundry bleaches are aqueous solutions of sodium hypochlorite (NaOCl). These formulations generally have 4.25% NaOCl, yet they vary widely in price. Such price variations in standardized products usually result from costly advertisement of the more familiar brand name products. Consumers would be wise to read the lists of ingredients on labels of competitive brands and then compare prices.

Bleaching powder [$Ca(OCl)_2$] is generally preferred for large-scale bleaching operations. The paper industry uses it to make white paper, and the textile industry uses it to make whiter fabrics.

In both aqueous bleaches and bleaching powder the active agent is the hypochlorite ion (ClO^-). Materials appear colored because loosely bound electrons are boosted to higher energy levels by absorption of visible light (section 2.10). Bleaching agents do their work by removing or tying down

Figure 8.8 Two familiar oxidizing agents and uses thereof.

these mobile electrons. For example, hypochlorite ion (in water) takes up electrons to form chloride ions and hydroxide ions.

$$ClO^- + H_2O + 2\ e^- \longrightarrow Cl^- + 2\ OH^-$$

Hypochlorite bleaches are safe and effective for cotton and linen fabrics. They should not be used for wool, silk, or nylon.

Other bleaching agents include hydrogen peroxide, sodium perborate (often formulated $NaBO_2 \cdot H_2O_2$ to indicate a complex of $NaBO_2$ and H_2O_2), and a variety of chlorine-containing organic compounds that release chlorine molecules in water. When hydrogen peroxide is used to bleach hair, it acts as an oxidizing agent. In the process, the black or brown pigment in the hair, called melanin, is oxidized to colorless products.

Stain removal is not nearly so simple a process as bleaching. A few stain removers are oxidizing agents or reducing agents; others have quite different chemical natures. Nearly all stains require rather specific stain removers. Hydrogen peroxide in cold water removes blood stains from cotton and linen fabrics. Potassium permanganate will remove most stains from white fabrics (except for rayon). The permanganate stain can then be removed by treatment with oxalic acid.

$$\underset{\textit{Oxalic acid}}{5\ H_2C_2O_4} + \underset{\textit{(Purple)}}{2\ MnO_4^-} + 6\ H^+ \longrightarrow \underset{\textit{(Colorless)}}{10\ CO_2 + 2\ Mn^{2+}} + 8\ H_2O$$

(Oxalic acid also removes rust spots, but its action in this case is as a complexing agent, not a reducing agent. The oxalic acid picks up the otherwise insoluble rust and carries it in solution to be washed away.)

Sodium thiosulfate ($Na_2S_2O_3$) readily removes iodine stains by reducing iodine to a colorless ion (I^-).

$$\underset{\textit{(Brown)}}{I_2} + 2\ Na_2S_2O_3 \longrightarrow \underset{\textit{(Colorless)}}{2\ NaI + Na_2S_4O_6}$$

Many stain removers are simply adsorbants (e.g., cornstarch, which removes grease spots), solvents (e.g., amyl acetate or acetone, which removes ballpoint ink), or detergents (which remove mustard stains).

.10 Oxidation, Reduction, and Living Things

Living organisms obtain energy for physical and mental activities by the low, multistep oxidation of food. These processes will be discussed in deail in later chapters, but for now we will represent them schematically as 'ollows.

$$\text{Carbohydrates (sugars and starches)} + O_2 \longrightarrow CO_2 + H_2O + \text{energy}$$

$$\text{Fats} + O_2 \longrightarrow CO_2 + H_2O + \text{energy}$$

$$\text{Proteins} + O_2 \longrightarrow CO_2 + H_2O + \text{urea}^* + \text{energy}$$

Green plants make these foods by reduction of carbon dioxide and water, and we eat either the plants or the animals which the plants feed. Energy for the reduction reaction, called photosynthesis, comes from the sun. The process, shown here for the formation of glucose, a simple sugar, may be written

$$6\ CO_2 + 6\ H_2O + \text{energy} \longrightarrow C_6H_{12}O_6 + 6\ O_2$$

This reaction is precisely the reverse of the first oxidation reaction (above). If the sugar is glucose, the oxidation is

$$C_6H_{12}O_6 + 6\ O_2 \longrightarrow 6\ CO_2 + 6\ H_2O + \text{energy}$$

We can see that green plants are the reducing agents that make possible all life on earth. Animals are oxidizing agents, able to survive only because plants provide the materials which are oxidized. We might therefore consider crop farming a process of reduction. Energy captured in cultivated plants, whether the plants are used directly or are fed to animals, is the basis for human life. If plants couldn't reduce, and if we couldn't oxidize, there would be no life.

Example 8.9 Calculate the oxidation state of carbon in carbon dioxide (CO_2) and in glucose ($C_6H_{12}O_6$).

The oxidation state of carbon in CO_2 is +4. In $C_6H_{12}O_6$ it may be calculated as follows.

$$6x + 12(+1) + 6(-2) = 0$$

$$6x + 12 - 12 = 0$$

$$6x = 0$$

$$x = 0$$

Now can you see how green plants are reducing agents and how we and other animals are oxidizing agents?

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*In some organisms, the nitrogen winds up as ammonia (NH_3) rather than as urea.

Problems

1. Write the formula for the products formed when each of the following burns (i.e., reacts with oxygen).
   a. $CH_4 + O_2 \rightarrow$
   b. $C + O_2 \rightarrow$
   c. $S + O_2 \rightarrow$
   d. $CS_2 + O_2 \rightarrow$
2. Assign oxidation numbers to the underlined elements.
   a. $\underline{S}_8$
   b. $\underline{S}O_3$
   c. $H_2\underline{S}$
   d. $K\underline{I}$
   e. $\underline{Al}_2O_3$
   f. $H\underline{N}O_2$
   g. $Na_2\underline{S}O_3$
   h. $NaH\underline{C}O_3$
   i. $H\underline{P}O_2^-$
   j. $\underline{U}O_2^{2+}$
3. Circle the oxidizing agent and underline the reducing agent in these reactions.
   a. $Cl_2 + 2\,KBr \rightarrow 2\,KCl + Br_2$
   b. $4\,Al + 3\,O_2 \rightarrow 2\,Al_2O_3$
   c. $C_2H_4 + H_2 \rightarrow C_2H_6$
   d. $2\,SO_2 + O_2 \rightarrow 2\,SO_3$
   e. $Fe + 2\,HCl \rightarrow FeCl_2 + H_2$
   f. $2\,HNO_3 + SO_2 \rightarrow H_2SO_4 + 2\,NO_2$
   g. $5\,C_2H_5OH + 4\,MnO_4^- + 12\,H^+ \rightarrow 5\,CH_3COOH + 4\,Mn^{2+} + 11\,H_2O$
4. Define oxidation and reduction in terms of the following.
   a. oxygen atoms gained or lost
   b. hydrogen atoms gained or lost
   c. electrons gained or lost
   d. change in oxidation number
5. List four common oxidizing agents.
6. List three common reducing agents.
7. Describe how a bleaching agent such as hypochlorite (ClO^-) works.
8. How can hydrogen peroxide act as both an oxidizing agent and a reducing agent?
9. In what sense are we oxidizing agents and green plants reducing agents?

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chapter 9

Solutions

You are a solution of sodium ions, potassium ions, calcium ions, bicarbonate ions, chloride ions, glucose, amino acids, fatty acids, glycerol, fats, proteins, acetylcholine, and lots of other goodies. Well, you aren't all in solution, or else you would wash away in the shower. But, except for a few semisolid parts, such as skin and muscle and bone, you are mostly water.* The rest of you is floating around in that water.

Almost all living systems are made up of thin chemical "soups" in contact with membranes and small cellular parts called organelles. The membranes and organelles are made up of complex chemicals called lipids (fats and fatlike substances), carbohydrates (sugars, starches, and cellulose), proteins, and nucleic acids (DNA and RNA). Life processes occur in solutions and at the interfaces between solutions and semisolid organelles and membranes. Although the chemistry of these processes is now being rapidly unraveled, it is still poorly understood. Therefore, in this chapter we will deal mainly with the simpler solutions.

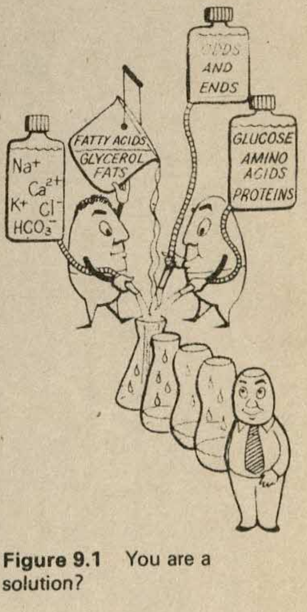

Figure 9.1 You are a solution?

9.1 Solutions for All Seasons: Definitions and Types

Put a teaspoon of sugar in a cup of water. Stir until all the sugar is dissolved. Taste the sweetened water from one side of the cup and then from the other. Use a straw to taste it from the center and then from the bottom. If you did a proper job of mixing, the water has the same degree of sweetness throughout; that is, it is *homogeneous*. You could have added more sugar to make the water sweeter, or you could have used less sugar to make it less sweet. Further, you could boil the water away and recover the sugar. The sugar and water have not reacted chemically. This mixture of sugar in water

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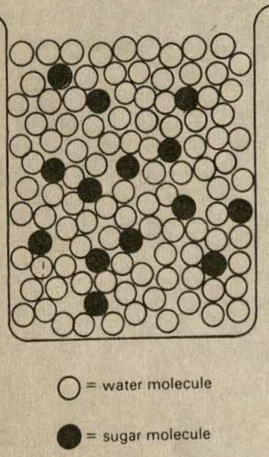
*The female body is 55% to 65% water, and the male body is 65% to 75% water. Those women who think men are all wet aren't too far wrong.

Figure 9.2 In a solution of sugar in water, the sugar molecules are randomly distributed among the water molecules.



is called a *solution*, and we say that the sugar is *dissolved* in the water. We can define a solution as a homogeneous mixture of two or more kinds of atoms, molecules, or ions. In a true solution, the mixture is intimate right down to the molecular level. There are *not* clumps of sugar molecules, but single molecules randomly distributed among the water molecules in much the same way that black marbles can be distributed among white ones (**figure 9.2**).

The components of a solution are given special names. The substance being dissolved (usually present in a lesser amount) is called the *solute*. The substance doing the dissolving (usually present in a greater amount) is called the *solvent*. Water is undoubtedly the most familiar solvent, and it dissolves many familiar substances such as sugar, salt, and alcohol. There are many other solvents. Gasoline dissolves grease. Many drugs are dissolved in alcohol. Banana oil is a solvent for the glue used in making model airplanes. In this chapter, though, we will deal for the most part with *aqueous* solutions, those in which the solvent is water.

A solvent need not be a liquid. Air is a solution of oxygen, argon, water vapor, and other gases in nitrogen gas. Steel is a solution of carbon (the solute) in iron (the solvent)—a solid in a solid.

In aqueous solutions, the solute may be a liquid, a gas, or a solid. Vinegar is a solution of acetic acid (a liquid) in water. Champagne and soda pop have a gas (carbon dioxide) in aqueous solution. Sugar and salt are examples of solids which dissolve in water. Blood plasma is an aqueous solution of solids (e.g., salt), liquids (e.g., alcohol, if you've been drinking), and gases (e.g., oxygen and carbon dioxide). To understand these more complex systems, let's first try to understand some simpler ones.

9.2 Qualitative Aspects of Solubility: A Pinch in a Pint

We say that sugar is *soluble* in water. Just what does that mean? Can we dissolve a teaspoon of sugar in a cup of water? Can we dissolve 10 teaspoons, or 100 teaspoons? We know from everyday experience that there is a limit to the amount of sugar we can dissolve in a given volume of water. Nevertheless, we still find it convenient to say that sugar is soluble in water, for we can dissolve an appreciable amount.

There are a few substances which can be mixed in all proportions. Water and alcohol are familiar examples. We say that such substances are completely *miscible*. For most "soluble" compounds, though, there is a limit to the amount that will dissolve in a given solvent. Sometimes that limit is near zero. Put an iron nail in a beaker of water. There is no apparent change. We say that iron is *insoluble* in water. Even insolubility is relative, however. If we had a method sensitive enough, we would find that some iron had dissolved. The amount might well be regarded as insignificant, and that is the sense in which the term *insoluble* is used. We will find terms such as *soluble* and *insoluble* useful, but they are imprecise and must be used with care.

Two other imprecise but sometimes useful terms are *dilute* and *concentrated*. A dilute solution is one which contains a little bit of solute in lots of solvent. A concentrated solution is one in which lots of solute is dissolved in a relatively small amount of solvent. If we dissolved a few millilitres of ethylene glycol, or antifreeze (chapter 16), in several litres of water, the dilute solution would be quite "thin"—little changed in appearance from that of pure water. However, if we dissolved 1 ℓ of ethylene glycol in 1 ℓ of water, the concentrated solution would be rather syrupy—similar to pure ethylene glycol in consistency.

The terms *dilute* and *concentrated* are used in a quantitative way for solutions of acids and bases. We will specify their meanings in this context in the next chapter.

9.3 What Dissolves What and Why? Ionic Compounds

In chapter 7, we saw that the unique structure of water not only results in relatively strong forces between water molecules but also enables water to dissolve ionic compounds. Further, we examined the different types of forces that exist between identical molecules in pure liquids. Now let's look at the types of forces that exist between the solute and solvent molecules in solutions. The solubility of a given solute depends on the relative attraction between particles in the pure substances and in the solution.

Water is a good solvent for compounds of the Group IA elements. Most lithium, sodium, and potassium salts are quite soluble in water. Examples are sodium chloride (NaCl), sodium sulfate (Na_2SO_4), potassium phosphate (K_3PO_4), and lithium bromide (LiBr). Further, nearly all nitrate salts are soluble, as are salts which incorporate the ammonium ion. Silver nitrate ($AgNO_3$), mercury(II) nitrate [$Hg(NO_3)_2$], aluminum nitrate [$Al(NO_3)_3$], ammonium chloride (NH_4Cl), ammonium sulfate [$(NH_4)_2SO_4$], and ammonium phosphate [$(NH_4)_3PO_4$] are examples. Why do these compounds dissolve in water? At the end of chapter 7 (p. 163), we attempted to picture how water dissolves a salt such as sodium chloride. In essence, three things must happen. The attractive forces holding the salt ions together must be overcome. Similarly, the attractive forces holding at least some of the water molecules together must be overcome. Finally, the solute and solvent molecules must interact; that is, they must attract one another. Hydration (the process in which water molecules surround the solute ions) occurs when the energy released by the interaction of solute with solvent is greater than that needed to overcome the forces holding the ions together in the crystal lattice and the forces between the solvent molecules.

$$\text{Hydration of ions} > \begin{array}{c}\text{separation of}\\ \text{solvent molecules}\\ +\\ \text{breakdown of lattice}\end{array} = \text{soluble}$$

Energy released *Energy absorbed*

In some solids, the forces holding the ions together are so strong that they cannot be overcome by the hydration of the ions. Many solids in which both ions are doubly or triply charged are essentially insoluble in water. Examples are calcium carbonate (Ca^{2+} and CO_3^{2-}), aluminum phosphate (Al^{3+} and PO_4^{3-}), and barium sulfate (Ba^{2+} and SO_4^{2-}). The large electro-static forces between the ions hold the particles together despite the attraction of solvent molecules.

$$\text{Hydration of ions} < \begin{array}{c}\text{separation of}\\ \text{solvent molecules}\\ +\\ \text{breakdown of lattice}\end{array} = \text{insoluble}$$

Energy released *Energy absorbed*

Table 9.1 summarizes the solubilities of a variety of ionic compounds.

Table 9.1
Solubilities of solid ionic compounds in pure water

	NO_3^-	CH_3COO^-	Cl^-	SO_4^{2-}	OH^-	S^{2-}	CO_3^{2-}	PO_4^{3-}
NH_4^+	S*	S	S	S	N	S	S	S
Na^+	S	S	S	S	S	S	S	S
K^+	S	S	S	S	S	S	S	S
Ba^{2+}	S	S	S	I	S	D	I	I
Ca^{2+}	S	S	S	P	P	P, D	I	I
Mg^{2+}	S	S	S	S	I	D	I	I
Cu^{2+}	S	S	S	S	I	I	I	I
Fe^{2+}	S	S	S	S	I	I	I	I
Fe^{3+}	S	N	S	P	I	D	N	I
Zn^{2+}	S	S	S	S	I	I	I	I
Pb^{2+}	S	S	P	I	I	I	I	I
Ag^+	S	P	I	I	N	I	I	I
Hg_2^{2+}	S, D	P	I	I	N	I	I	I
Hg^{2+}	S	S	S	D	N	I	N	I

*The letters are defined as follows.

S = is soluble in water
P = is partially soluble in water
I = is insoluble in water
D = decomposes
N = does not exist as an ionic solid

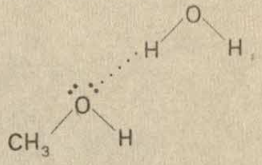
9.4 What Dissolves What and Why? Covalent Compounds

An old but helpful rule states that like dissolves like. This means that nonpolar (or only slightly polar) solutes dissolve best in nonpolar solvents and that polar solutes dissolve best in polar solvents. The rule works well for nonpolar substances. Fats, oils, and greases (nonpolar or only slightly polar) dissolve well in nonpolar solvents such as benzene. The forces which hold nonpolar molecules together are generally weak. Thus, the amount of

The importance of water as a solvent is reflected in the number of terms which have been coined to describe systems involving water. For example, the general term for the interaction of solvent with solute is *solvation*, but there is a special term for the interaction of water with a solute—*hydration*. Certain compounds, such as calcium sulfate, tend to hold on to some water molecules even when they crystallize from solution. These compounds with their bound water molecules are called *hydrates*. The formulas for these crystals are written in such a way as to indicate the number of attached water molecules. Plaster of Paris is $(CaSO_4)_2 \cdot H_2O$ (one water molecule for every two calcium sulfate units). If more water is available, $CaSO_4 \cdot 2H_2O$ is formed (now there are two water molecules for every $CaSO_4$ molecule). When a plaster cast is formed to immobilize a broken bone, the first hydrate is converted to the second. The powdery plaster of Paris changes to the rigid, protective material of the cast.

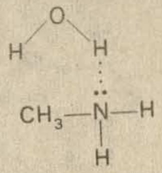
If a hydrate is heated strongly enough, the bound water can be driven off to produce the *anhydrous* compound, that is, the compound without water. Some hydrates lose their bound water simply on standing in dry air. Such compounds are said to be *efflorescent*. Other compounds form hydrates by picking up water from the atmosphere. These are described as *hygroscopic*. And finally, some compounds are so good at pulling water molecules from the air, that they eventually dissolve in the water thus accumulated. These compounds are said to be *deliquescent*.

energy needed to pull apart molecules of pure solute and to disrupt the attractive forces between molecules of pure solvent is small. And this energy can be balanced by that released through the interaction of solute and solvent molecules, although this too is slight.



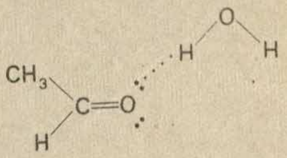
Methanol
(soluble in water)

Interaction of nonpolar solute with nonpolar solvent	>	separation of solvent molecules + separation of solute molecules	= solution
Energy released		*Energy absorbed*	



Methylamine
(soluble in water)

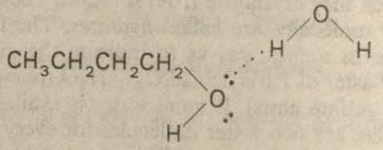
The rule that like dissolves like is not as helpful for polar substances and, in particular, for aqueous solutions. The important thing for water solubility is the ability of water to form hydrogen bonds to the solute molecules. Thus, molecules containing a high proportion of nitrogen or oxygen atoms will dissolve in water because these are the elements which can form hydrogen bonds. One example is methanol, also called methyl alcohol (CH_3OH), which is completely miscible with water. Methylamine (CH_3NH_2) is also quite soluble in water.



Acetaldehyde
(soluble in water)

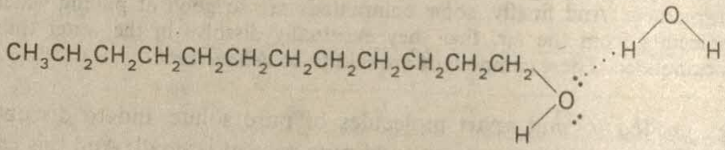
There need not be a hydrogen atom on the oxygen (or nitrogen) atom of the solute molecules. Acetaldehyde (CH_3CHO) is completely miscible with water even though none of the hydrogen atoms in the molecule is attached to the oxygen (see structure at right). The hydrogen bonds depicted in the drawing incorporate hydrogen atoms covalently bonded to the oxygen of the water molecules.

Each nitrogen or oxygen atom in a solute molecule can carry along into solution about 4 attached carbon atoms. For alcohols (carbon-containing compounds containing the —OH group), those with 3 or fewer carbons are completely miscible with water. *n*-Butyl alcohol ($CH_3CH_2CH_2CH_2OH$) is only partially soluble.

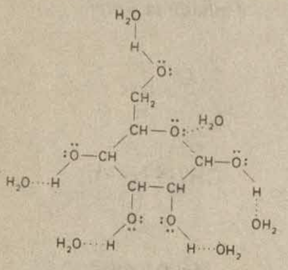


n-*Butyl alcohol (partially soluble in water)*

And a compound with 12 carbon atoms and only 1 oxygen is essentially insoluble. In its solubility, this molecule reflects the character of the nonpolar chain of carbons and hydrogens, rather than that of the single oxygen atom.



Lauryl alcohol
(essentially insoluble in water)



Glucose
(soluble in water)

Some fairly complex molecules, such as those of the sugars, are quite soluble in water. Glucose, or blood sugar ($C_6H_{12}O_6$), contains 6 carbon atoms, but its 6 oxygen atoms permit it to hydrogen bond to many water molecules and, thus, confer on it water solubility.

Hydrogen bonding, then, is the important factor in water solubility. Polarity alone is not enough. Methyl chloride (CH_3Cl) and methyl alcohol (CH_3OH) have about the same polarity, yet methyl chloride is essentially insoluble in water while methyl alcohol is completely miscible with water. Methyl chloride does not engage in hydrogen bonding and methyl alcohol does. A few polar substances, such as hydrogen chloride (HCl), dissolve in water because they react to form ions; these will be discussed in subsequent chapters.

9.5 Dynamic Equilibria: The More Things Change . . .

For most substances, there is a limit to how much can be dissolved in a given volume of solvent. This limit varies with the nature of the solute and

For some stains, such as that produced by blood, cold water is recommended. In this case, hot water causes a change in the structure of certain elements in the blood which makes these more *insoluble*. Cold water does not change the blood in this way, and it is for this reason that cold water is recommended.

of the solvent. Solubility also varies with temperature, generally (but not always) increasing with increasing temperature. We usually wash our clothes in hot water because most forms of "dirt" are more soluble at higher temperatures.

Solubilities are often expressed in terms of grams of solute per 100 g of solvent. Since solubility varies with temperature, it is necessary to indicate the temperature at which the solubility is measured. For example, 100 g of water will dissolve up to 109 g of sodium hydroxide (NaOH) at 20 °C. At 50 °C, 145 g of NaOH will dissolve in 100 g of water. In a shorthand method, the solubility of sodium hydroxide is expressed as 109^{20} and 145^{50} (the 100 g of water is understood).

The solubility of sodium chloride, or common table salt (NaCl), is 36 g per 100 g of water at 20 °C. Suppose that we place 40 g of NaCl in 100 g of water. What happens? Initially, many of the sodium (Na^+) ions and chloride (Cl^-) ions leave the surface of the crystals and wander about at random through the solvent. Some of the ions in their wanderings return to a crystal surface. These ions can even be trapped there, becoming once more a part of the crystal lattice. As more and more salt dissolves, the number of "wanderers" which return to be trapped once again in the solid state increases. Eventually (when 36 g of NaCl has dissolved), the number of ions leaving the surface of the undissolved crystals will just equal the number returning. A condition of *dynamic equilibrium* will have been established. The *net* amount of sodium chloride in solution will remain the same despite the fact that there is still a lot of activity as ions come and go from the surface of the crystals. The net amount of undissolved crystals also remains constant (in this example, 4 g), although individual crystals may change in shape and size as ions leave one part of the crystal to enter solution while others are deposited at another part of the lattice. Some small crystals may even disappear as others grow larger, yet the net amount of undissolved salt will not change. The rate of dissolution will just equal the rate of regrowth.

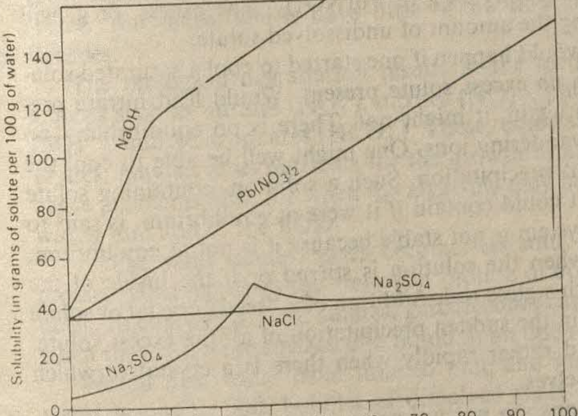


Figure 9.3 The effect of temperature on the solubility of several solids in water.

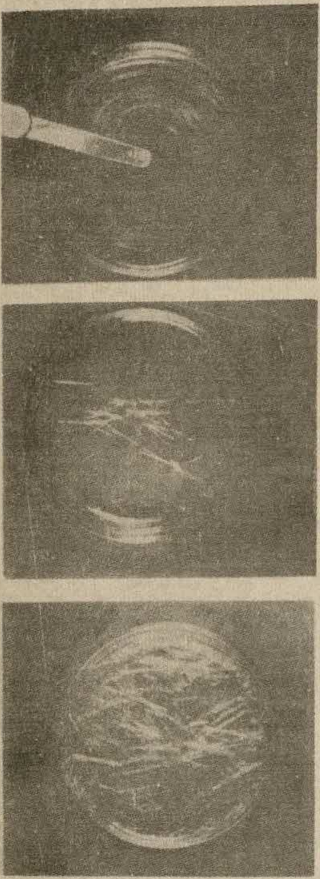


Figure 9.4 Addition of a seed crystal induces rapid crystallization of excess solute from a supersaturated solution. (Reprinted with permission from Keenan, Charles W., Wood, Jesse H., and Kleinfelter, Donald, *Genaral College Chemistry*, 5th ed., New York: Harper and Row, 1976. Copyright © 1976, 1971, 1966, 1961, 1957 by Harper and Row, Publishers, Inc.)

A solution which contains all the solute that it can at equilibrium and at a given temperature is said to be *saturated.* One that contains less than this amount is *unsaturated.* A solution with 24 g of NaCl in 100 g of water at 20 °C would be unsaturated because it could dissolve 12 g more at that temperature.

Equilibrium holds only for a given temperature. Consider once more a sodium hydroxide solution. If we add 145 g of NaOH to 100 g of water, 109 g of the NaOH will dissolve at 20 °C, leaving 36 g as undissolved solute. If the solution is then warmed, more solute will dissolve. Finally, at 50 °C all 145 g of NaOH will be in solution. The solubility of sodium hydroxide increases with increasing temperature.

Most solid compounds are increasingly soluble as the temperature is raised (**figure 9.3**). This should not be surprising. As the temperature goes up, the motion of all the particles is increased. More ions are knocked loose from the lattice and go into solution. Further, it is more difficult for the crystal to recapture the ions which return to its surface, because they are moving at higher speeds. There are a few exceptions to this general rule of increased solubility at higher temperatures (see the graph of Na_2SO_4 in **figure 9.3**). These exceptions probably involve changes in the hydration of the ions as the temperature increases.

Notice that for some substances, such as sodium hydroxide (NaOH) and lead nitrate [$Pb(NO_3)_2$], solubility increases rapidly as the temperature increases. The solubility of sodium chloride (NaCl), in contrast, changes very little over the indicated range of temperatures. The solubility of sodium sulfate (Na_2SO_4) first increases rather rapidly and then decreases, indicating a change in the hydration of the sodium (Na^+) ions and the sulfate (SO_4^{2-}) ions.

If a saturated solution of lead nitrate (with excess solid lead nitrate present) is cooled, more solute precipitates until the equilibrium is once again established at the lower temperature. For example, consider a saturated solution of lead nitrate at 90 °C. For each 100 g of water there will be 120 g of $Pb(NO_3)_2$ dissolved. When the solution is cooled to 20 °C, the solution at equilibrium can contain only 54 g of $Pb(NO_3)_2$. The excess, 66 g, will precipitate out, increasing the amount of undissolved solute.

Now consider what would happen if one started to cool a saturated solution of lead nitrate with *no* excess solute present. Would lead nitrate precipitate? It might. Then again, it might not. There is no equilibrium—no crystals to capture the wandering ions. One might well be able to cool the solution to 20 °C without precipitation. Such a solution, containing solute in excess of that which it could contain *if* it were at equilibrium, is said to be *supersaturated.* This system is not stable because it is not at equilibrium. Solute may precipitate when the solution is stirred or if the inside of the container is scratched with a glass rod. Addition of a "seed" crystal of solute will nearly always result in the sudden precipitation of all the excess solute. Equilibrium is established rather rapidly when there is a crystal to which the ions can attach themselves.

Supersaturated solutions are not unknown in nature. Honey is one example; the solute is sugar. If honey is left to stand, the sugar crystallizes.

We say, not very scientifically, that the honey has "turned to sugar." Supersaturated sugar solutions are fairly common in cooking. Jellies are one example. The sugar often crystallizes from jelly that has been standing for a long time.

Some cosmetics, the "pearly" hand creams, for example, also make use of supersaturated solutions. Stearic acid (chapter 18) is dissolved in a hot mixture of oil, glycerol, and water. The mixture is then cooled and packaged. After several days of standing, the stearic acid crystallizes, giving the cream its characteristic pearly appearance.

9.6 Solutions of Gases in Water: Soda Pop and Pressure, Temperature and Trout

You are no doubt familiar with a number of solutions in which gases are dissolved in water. Soda pop is a solution of carbon dioxide (and flavoring and sweetening agents) in water. Blood contains dissolved oxygen and carbon dioxide. Familiar household cleansers include those with ammonia (NH_3) dissolved in water. Formalin, used as a biological preservative, is an aqueous solution of formaldehyde (HCHO). Natural waters contain dissolved oxygen. Although only slightly soluble in water (0.0043 g of O_2 will dissolve in 100 g of water at 20 °C), this oxygen is vital to the survival of fish and other aquatic species.

Organic wastes such as sewage, when dumped into rivers, lakes, and streams, often deplete the amount of dissolved oxygen, which results in the subsequent death of fish. Most, but not all, organic material can be broken down by microorganisms. These bacteria use up the dissolved oxygen in oxidizing the organic matter. A measure of the amount of oxygen needed for this degradation is the *biochemical oxygen demand* (BOD). The greater the quantity of degradable organic wastes, the higher the BOD. If the BOD is high enough, no life (other than odor-producing anaerobic microorganisms which multiply in the absence of dissolved oxygen) can survive in the lake or stream.

Flowing streams can regenerate themselves. Rapid ones soon come alive again as oxygen from the atmosphere is dissolved by the moving water. But lakes, which have little or no flow, may remain "dead" for decades.

The biological degradation results in the formation of inorganic substances such as nitrates (NO_3^-), nitrites (NO_2^-), phosphates (PO_4^{3-}), sulfates (SO_4^{2-}), and bicarbonates (HCO_3^-). These, especially the nitrates and phosphates, may serve as nutrients for the growth of algae. The algal "blooms" cause problems also, for when the algae die they become part of the organic wastes and add to the BOD.

Unlike solid solutes, gases become less soluble as the temperature increases. Heat increases the molecular motion of both solute and solvent particles. In contrast to solid solutes, gaseous ones can escape from the solution when they reach the surface of a liquid in an open container.

We all heat water from time to time and know that, long before the water begins to boil, bubbles of dissolved gases appear (**figure 9.5**). These soon rise to the surface and escape into the atmosphere. **Figure 9.6** shows

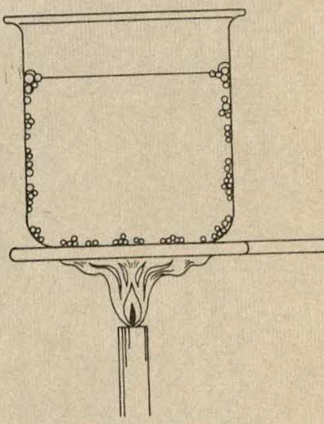


Figure 9.5 Bubbles of air form when a beaker of water is heated.

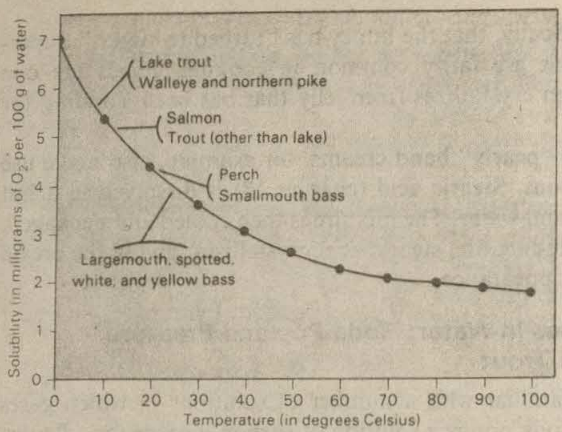


Figure 9.6 The solubility of oxygen at various temperatures at 1 atm of pressure. Also shown are maximum temperatures at which spawning and egg development for various species of fish occur.

the effect of temperature on the solubility of oxygen in water. Also shown are the effect of temperature and consequent oxygen content on the spawning and egg development of several species of game fish. More sluggish fish, such as carp, gar, and catfish, can reproduce at higher temperatures, presumably because they require less oxygen.

The solubility of gases in water also varies with the pressure of the gas. The higher the pressure, the more gas one can dissolve in a given amount of water. **Figure 9.7** shows how the solubility of oxygen in water at 25 °C varies with pressure.

Soda pop consists of carbon dioxide dissolved in sweetened, flavored water under pressure. Once the container is opened, the pressure is reduced. Carbon dioxide escapes, rapidly at first and then more slowly. Eventually most of the gas is gone; the beverage has gone "flat."

9.7 Quantitative Aspects of Solubility: Moles and Milligrams

Most reactions of interest to us, including those in our bodies, take place in solution. A good cook may well get by with concentrations expressed as

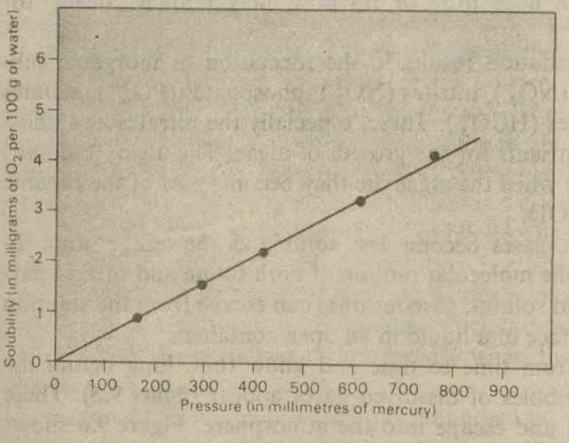


Figure 9.7 The effect of pressure on the solubility of oxygen in water.

"a pinch of salt in a pint of water," but scientific work generally requires more precise measurement of amounts. We have already discussed the measurement of solubility in grams of solute per 100 g of solvent. Since substances react in small whole-number ratios of molecules or ions (chapter 5), it is often convenient to measure the amount of solute in moles. The amount of solution is usually measured in litres or millilitres. A solution which contains 1 mole of solute per litre of solution is called a 1 *molar* (or 1 *M*) solution. *Molarity*, then, is defined as the number of moles of solute divided by the number of litres of solution.

$$\text{Molarity } (M) = \frac{\text{moles of solute}}{\text{litres of solution}}$$

Example 9.1 What is the molarity of a solution made by dissolving 3 moles of NaCl in enough water to make 6 ℓ of solution?

$$\frac{3 \text{ moles of solute}}{6 \text{ litres of solution}} = 0.5\ M$$

Recall that the number of moles of a substance is calculated by division of mass in grams by formula weight in grams per mole.

$$\text{Moles} = \frac{\text{mass}}{\text{formula weight}}$$

The formula weight of NaOH is $23 + 16 + 1 = 40$. In 120 g of NaOH there would be $120 \div 40 = 3$ moles of NaOH.

Example 9.2 What is the molarity of a solution of 300 g of $KHCO_3$ in enough water to make 10 ℓ of solution?

The formula weight of $KHCO_3$ is $39 + 1 + 12 + (3 \times 16) = 100$. The number of moles of $KHCO_3$ is $300 \div 100 = 3$. The molarity of the solution is

$$\frac{3 \text{ moles}}{10\ \ell} = 0.3\ M$$

Frequently one needs to know how much solute is required for the preparation of a specified amount of solution of a given molarity. Recall that

$$\text{Molarity} = \frac{\text{moles of solute}}{\text{litres of solution}}$$

We can rearrange this to get

$$\text{Moles of solute} = \text{molarity} \times \text{litres of solution}$$

Example 9.3 How many grams of NaOH (which has a formula weight of 40) are required for the preparation of 500 ml (0.5 ℓ) of 6 *M* solution?

We can use the rearranged equation to determine the number of *moles* of NaOH required.

$$\text{Moles of NaOH} = 6\ M \times 0.5\ \ell = \frac{6\text{ moles}}{1\ \ell} \times 0.5\ \ell = 3\text{ moles}$$

But we were asked for the number of grams and not moles, so we must now calculate the number of grams in 3 moles.

$$\text{Moles of NaOH} = \frac{\text{grams of NaOH}}{\text{formula weight of NaOH}}$$

Rearranging, we get

$$\text{Grams of NaOH} = \text{moles of NaOH} \times \text{formula weight of NaOH}$$

$$= 3\text{ moles} \times \frac{40\text{ g}}{1\text{ mole}} = 120\text{ g}$$

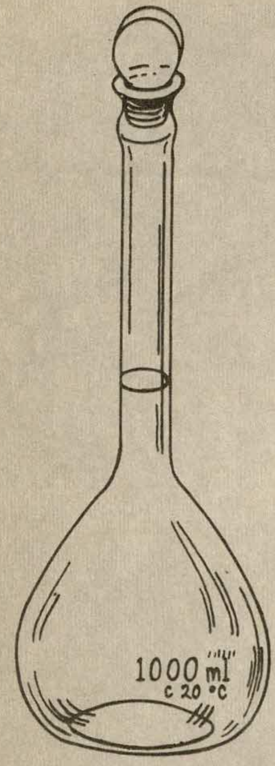


Figure 9.8 A volumetric flask. When filled to the mark on the neck, the flask contains 1000 ml (1 ℓ) of solution.

Quite often solutions of known molarity are available. How would you calculate the volume you would need in order to get a certain number of moles of solute? We can again rearrange the definition of molarity to obtain

$$\text{Litres of solution} = \frac{\text{moles of solute}}{\text{molarity}}$$

Example 9.4 How many litres of 12 M HCl solution would one have to take to get 0.48 mole of HCl?

$$\text{Litres of HCl solution} = \frac{0.48\text{ moles HCl}}{12\ M} = \frac{0.48\text{ moles HCl}}{12\text{ moles HCl}/\ell} = 0.04\ \ell$$

We would need 0.04 ℓ (40 ml) of the solution to have 0.48 mole.

Remember that molarity is moles per litre of *solution*, not per litre of solvent. To make a litre of a 1 M solution, one weighs out 1 mole of solute and places it in a volumetric flask, which is a standard piece of laboratory glassware designed to contain a precisely specified volume of liquid (**figure 9.8**). Enough water is added to dissolve the solute, and then more water is added to bring the volume up to the mark which indicates 1 ℓ of *solution*. (Simply adding 1 mole of solute to 1 ℓ of water would, in most cases, give more than 1 ℓ of solution.)

For many purposes, it is not necessary to know the number of moles of solute but only the relative amounts of solute and solvent. One way of expressing this is in terms of the percent of solute. If both the solute and solvent are liquids, *percent by volume* is used.

$$\text{Percent by volume} = \frac{\text{volume of solute}}{\text{volume of solute + solvent}} \times 100$$

Example 9.5 What is the percent by volume of a solution of 100 ml of alcohol dissolved in 300 ml of water?

$$\text{Percent by volume} = \frac{100 \text{ ml of alcohol}}{100 \text{ ml of alcohol} + 300 \text{ ml of water}} \times 100$$

$$= \frac{100 \text{ ml}}{400 \text{ ml}} \times 100 = 25\%$$

Example 9.6 What volume of alcohol and water must one mix to obtain about 200 ml of a 40%-by-volume solution of alcohol in water?

$$40\% = \frac{\text{millilitres of alcohol}}{200 \text{ ml total volume}} \times 100$$

Rearranging, we get

$$\text{Millilitres of alcohol} = \frac{40 \times 200}{100} = 80 \text{ ml of alcohol}$$

To find the amount of water required, subtract the volume of alcohol from the total volume.

$$200 \text{ ml} - 80 \text{ ml} = 120 \text{ ml of water}$$

When the 80 ml of alcohol is mixed with 120 ml of water, the total volume may not be exactly 200 ml, but it will be very close.

For solutions involving solutes which are solids, a more commonly used relationship is *percent by weight*.

Example 9.7 What is the percent by weight of a solution of 5 g of NaCl dissolved in 495 g (495 ml) of water?

$$\text{Percent by weight} = \frac{5 \text{ g}}{495 \text{ g} + 5 \text{ g}} \times 100 = \frac{5 \text{ g}}{500 \text{ g}} \times 100 = 1\%$$

Note that, since 1 ml of water weighs 1 g, one can obtain 495 g of water simply by measuring 495 ml of water.

Example 9.8 How would you prepare about 100 ml of a 5% NaOH solution?

For dilute aqueous solutions, the density of the solution is approximately equal to the density of water. Therefore, let's assume that 100 ml of the solution will weigh about 100 g.

$$5\% = \frac{\text{grams of NaOH}}{100 \text{ g total}} \times 100$$

Rearranging, we get

$$\text{Grams of NaOH} = \frac{5 \times 100}{100} = 5 \text{ g}$$

Percent means "parts per hundred." To make a hundred "parts" of solution, weigh out 5 g of NaOH. Add 95 g (95 ml) of water. (The final volume might not be exactly 100 ml, but it will be close to that.)

Example 9.9 How would you prepare about 500 ml of a 10% $NaHCO_3$ solution?

$$10\% = \frac{\text{grams of NaHCO}_3}{500 \text{ g total}} \times 100$$

Rearranging, we get

$$\text{Grams of NaHCO}_3 = \frac{10 \times 500}{100} = 50 \text{ g}$$

Weigh out 50 g of $NaHCO_3$ and dissolve it in 500 − 50 = 450 g (450 ml) of water. Again, the total volume will be about, rather than exactly, 500 ml.

Let us call attention to a special aspect of percent concentrations. If you are trying to calculate how much solute to weigh out for a particular percent concentration, it makes no difference what the solute is. A 10% solution of NaOH contains 10 g of NaOH per 100 g of total solution. Similarly, 10% HCl and 10% $(NH_4)_2SO_4$ and 10% $C_{110}H_{190}N_3O_2Br$ each contain 10 g of the specified solute per 100 g of solution. For molar solutions, however, the weight of solute in a solution of specified molarity is different for different solutes. A litre of a 0.1 *M* solution requires 4 g (0.1 mole) of NaOH, 3.7 g (0.1 mole) of HCl, 13.2 g (0.1 mole) of $(NH_4)_2SO_4$, and 166 g (0.1 mole) of $C_{110}H_{190}N_3O_2Br$.

Low concentrations of solutes, such as those in blood and urine, are often expressed in *milligram percent*, which is defined as milligrams per 100 ml of solution.

$$\text{Milligram percent} = \frac{\text{milligrams of solute}}{100 \text{ ml of solution}}$$

For example, normally there are about 320 to 350 mg of sodium ion per 100 ml of blood plasma. Thus, the normal concentration of sodium ion in blood plasma ranges from 320 to 350 mg %. The use of milligram percent avoids the sometimes cumbersome use of decimal numbers. For example, the above concentrations of sodium ion would be expressed as 0.320% to 0.350% by weight.

For some dilute solutions, concentrations are often expressed in parts per million (ppm) or even parts per billion (ppb). For aqueous solutions, ppm is the same as milligrams per litre (mg/ℓ) and ppb is identical to micrograms per litre (μg/ℓ). These units are frequently used to measure extremely low levels of toxic materials. Current concern over the purity of our drinking water centers on minute amounts of potentially dangerous compounds. For example, chloroform is a suspected carcinogen, that is, a cancer-causing substance. Studies made in 1975 on the water supply of Dallas, Texas, revealed a chloroform level of 18 ppb (equivalent to 1 drop in 733 gal). This was not considered a dangerous level, but the Environmental Protection Agency continues to monitor water purity as a protective measure.

Often solutions are available in concentrated form and must be diluted for use. Sometimes directions say, for example, dilute 1:3000. This means, add 1 part of the concentrated form to 3000 parts of solvent. Similarly, to dilute 1:3 means to add 1 part of the concentrated form to 3 parts of solvent. A solution made by a 1:3 dilution is a thousand times *more concentrated* than a 1:3000 one. The larger number refers to a *more dilute* preparation.

We will make extensive use of these various ways of expressing concentration in succeeding chapters.

9.8 Properties of Solutions: How to Elevate Your Boiling Point

Solutions have a variety of characteristic properties. The particles are molecules, atoms, or ions. Once the solute and solvent are thoroughly mixed, the *solute does not settle out*. Molecular motion keeps the particles randomly distributed. The sugar in a bottle of pop, for instance, does not settle to the bottom on standing. The last drop is just as sweet as, but no sweeter than, the first. You cannot get the sugar out by passing the pop through a piece of filter paper. The sugar molecules go through the pores of the paper as readily as the water molecules. All true solutions can be filtered without removal of the solute.

Solutions may be colored, but they are *clear* and *transparent*. Copper sulfate ($CuSO_4$), dissolved in water, gives a beautiful clear blue solution. A beam of light will shine right through the solution but will not be visible in the solution. When the path of light through a solution is visible, then particles larger than those in solution are present (section 9.10).

Another property of solutions of nonvolatile solutes is that they have a *lower vapor pressure* than the pure solvent. Nonvolatile solute particles prevent some of the solvent from escaping into the vapor phase. Some of the nonvolatile solute particles occupy positions at the liquid's surface (as well as throughout the solution). Therefore, there are fewer volatile molecules with the opportunity to escape from the surface to the vapor state. Lower vapor pressure results in *higher boiling points* for solutions of nonvolatile solutes. The solution must be raised to a higher temperature before the vapor pressure equals atmospheric pressure, that is, before the solution boils. For a solution of 1 mole of sugar in 1 kg of water, the boiling point is raised 0.51 °C. At standard pressure, such a solution would boil at 100.51 °C.

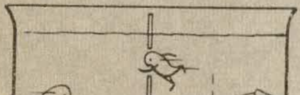
Perhaps more important than the elevation of boiling point is the behavior of solutions upon freezing. Addition of 1 mole of sugar to 1 kg of water lowers the freezing point by 1.86 °C. Ethylene glycol is added to automobile radiators to prevent the cooling water from freezing in winter. A mole (62 g) of glycol lowers the freezing point of 1 kg of water by 1.86 °C; 10 moles (620 g) lowers the freezing point by 18.6 °C. A mixture of 620 g of ethylene glycol and 1000 g (1 kg) of water, then, would not freeze until the temperature reached −18.6 °C (about −1 °F).

The amount the freezing point is depressed (or the amount the boiling

It is important to note that 1 mole of an ionic substance, such as sodium chloride or calcium chloride, will elevate the boiling point and depress the freezing point more than 1 mole of a molecular substance. This effect is related to the number of particles released in solution (the ionic compounds release separate positive ions and negative ions). We will discuss this further in chapter 12.

point is elevated) is characteristic of the solvent. It doesn't matter whether one dissolves 1 mole of sugar or 1 mole of ethylene glycol in 1 kg of water. The effect is the same: the freezing point is lowered by 1.86 °C. For a solvent other than water, the freezing point would be depressed by a different amount, one characteristic of that solvent. This is not to say the solute doesn't count at all. However, it is not what the solute is but how much of it is added. A mole of dissolved particles will depress the freezing point more than half a mole; it simply doesn't matter what the particles are.

Figure 9.9 The sieve theory of osmosis holds that the semipermeable membrane has pores large enough to permit the passage of water molecules (small creatures) but too small to permit the passage of larger molecules.



9.9 Solutions and Cell Membranes: Osmosis

In section 9.8 we saw that solutions—both solute and solvent—will go through filter paper. Another way to approach the phenomenon is to say that the paper is permeable to water and other solvents and to solutions. Everyday experience tells us that other materials are impermeable. Water and solutions will not pass through the metal walls of cans nor through the glass walls of jars and bottles. Are there, perhaps, materials with intermediate properties? Materials which will pass solvent molecules but not solute molecules? Materials which are permeable to some solutes but not others? The answer is an emphatic yes! Many natural membranes are *semipermeable*. Cell membranes, the lining of the digestive tract, and the walls of blood vessels are all semipermeable; they allow certain substances to go through while holding others back.

The sieve theory of *osmosis* holds that semipermeable membranes have extremely small pores through which tiny water molecules can pass but larger particles cannot. It is easy to picture how the small water molecule could squeeze through an opening too small to permit passage of sucrose ($C_{12}H_{22}O_{11}$, table sugar) (**figure 9.9**).

There is a lot of exciting research going on in the area of cell membranes. The best evidence we have today is that membranes are not just passive sieves but that they actively participate in the passage of molecules through the pores. For example, electronic charges on the surfaces of the pores undoubtedly interact with ions attempting to pass through. Nevertheless, the only really important thing for us at the moment is that semipermeable membranes pass some particles while blocking the passage of others.

Look again at **figure 9.9.** The left compartment contains pure water; the right, a sugar solution. Water molecules can pass through the membrane in either direction. Sugar molecules can't get through at all, yet those along the membrane can make it more difficult for water to go from right to left than from left to right. On both sides of the membrane all molecules are moving about at random, and occasionally they bump against the mem-

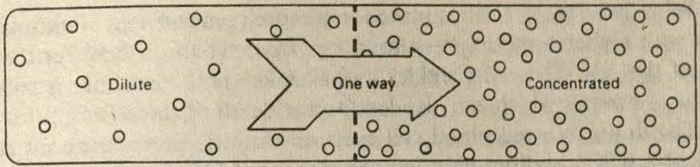


Figure 9.10 Net *solvent* flow through a semipermeable membrane goes spontaneously in only one direction, from the compartment containing dilute solution (or pure solvent) into the compartment of concentrated solution.

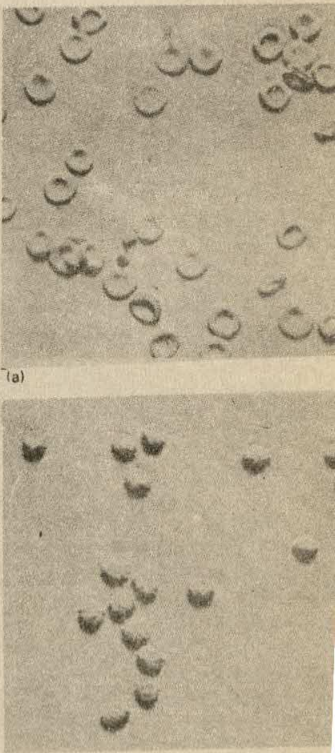
brane. If a bump involving a water molecule occurs at one of the pores, the water molecule will pass through. Sugar molecules treat the pores just like the walls and bounce back instead of through. The more sugar molecules there are in solution (i.e., the more concentrated the solution), the smaller the chances are that a given bump at a pore will involve a water molecule at the pore. Thus, in our example, there will be a *net* flow of water from the left compartment into the right compartment. The liquid level in the right compartment will rise until the push of the extra weight of water in that compartment is great enough to prevent further net flow of water into that compartment. As in so many processes we've described, things haven't come to a standstill; the rates at which water molecules move back and forth have just been equalized. Diffusion through a semipermeable membrane is called *osmosis*. During osmosis, there is always a *net* flow from the more dilute (or pure solvent) area to the compartment in which the solution is more concentrated **(figure 9.10)**.

As we have noted, osmosis (the net flow) will cease when the pressure of the water building up in one compartment becomes sufficiently high. Osmosis can also be stopped by application of external pressure to the side with the more concentrated solution. The precise amount of pressure needed to prevent the net flow of solvent from the dilute section to the concentrated one is called the *osmotic pressure*. The magnitude of the osmotic pressure depends only on the concentration of solute particles. The more particles—ions or molecules—the greater the osmotic pressure.

Cell membranes are generally not all-or-nothing sieves. They allow small molecules and ions, as well as solvent, to pass in both directions while holding back only the larger particles. Nevertheless, living cells can be regarded as selectively permeable bags. These are filled with ions, small and large molecules, and still larger cell components. In its normal environment, a cell is bathed in a fluid similar to its contents. Flow in and flow out are about equal. However, if the cell is placed in a new environment—inside or outside the body—drastic things may happen to it. If red blood cells, for example, are placed in pure water, there will be a net flow of water into the cell. The cell will become swollen. It may even burst.

In general, if a cell is placed in a solution of lower concentration or, more correctly, a solution with lower osmotic pressure (a *hypotonic* solution), more water will flow into the cell than out of it. The rupture of a cell by a hypotonic solution is called *plasmolysis*. If the cell is a red blood cell, the more specific term *hemolysis* is used. Plasmolysis, then, is the rupture of any cell; hemolysis is the rupture of a red blood cell.

Figure 9.11 (a) Normal human red blood cells. (b) After exposure to a hypertonic solution, the cells are wrinkled and shriveled. (Courtesy of A. M. Winchester, University of Northern Colorado, Greeley.)



What happens if a cell is placed in a more concentrated solution, a solution with higher osmotic pressure (a *hypertonic* solution)? Water then flows out of the cell. The cell wrinkles and shrinks. This shriveling is called *crenation*, a process which can also lead to the death of the cell.

The fluids in a red blood cell exert an osmotic pressure about equal to that of a 0.92% sodium chloride solution. Red blood cells placed in a salt solution of this concentration neither swell nor shrink, for the water flow in and the water flow out are equalized. Such solutions for which the osmotic pressure is the same as that of the fluid inside the cells are said to be *isotonic*.

In replacing body fluids intravenously, it is important that the fluid be isotonic with that inside the blood cells. Otherwise, hemolysis or crenation would result, and the patient's well-being would be seriously jeopardized. Solutions having 0.92% sodium chloride, called physiological saline, are often used. A solution containing 5.5% glucose (also called dextrose or blood sugar) is also isotonic with the fluid inside red blood cells. The "D5W" so often referred to on television's doctor shows is a 5% solution of dextrose (the *D*) in water (the *W*).

But isotonic solutions have limitations. Consider the case of a patient who is to be fed intravenously. There is a limit to the amount of water such a patient can handle in a day—about 3 ℓ. If an isotonic solution of 5.5% glucose were to be used, 3 ℓ of the solution would supply 165 g of glucose. This would yield 4 Cal/g to the patient, or a total of 660 Cal, an amount woefully inadequate. Even a resting patient requires about 1400 Cal per day. And for a person suffering from serious burns, for example, requirements

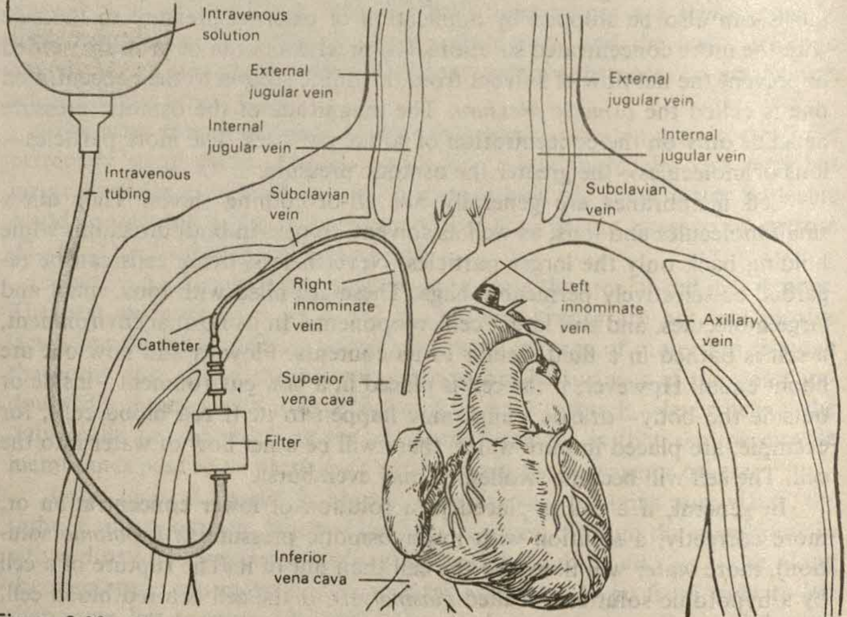


Figure 9.12 Concentrated nutrient solution may be infused directly into the superior vena cava. The solution is quickly diluted to near isotonic strength by the large volume of blood flowing through the vein.

as high as 10 000 Cal per day have been recorded. We have oversimplified the situation. Other vital nutrients are required by such patients, and, in fact, a person can normally be given up to 1200 Cal through carefully formulated solutions. This still falls short of the requirements of many seriously ill people. One answer to the problem is to use very concentrated solutions (about six times as concentrated as isotonic solutions). Instead of being administered through the vein of an arm or a leg, this solution is infused directly through a tube into the superior vena cava, a large blood vessel leading to the heart. The large volume of blood flowing through this vein quickly dilutes the solution to levels which will not damage the blood. With this technique, patients have been given 5000 Cal a day and have even gained weight.

9.10 Colloids: The In-between State

If sugar is dissolved in water, the molecules become intimately mixed. The solution is homogeneous; that is, it has the same properties throughout. The sugar cannot be filtered out by ordinary filter paper, nor does it settle out on standing. On the other hand, if one tries to dissolve sand in water, the two substances may momentarily appear to be mixed, but the sand rapidly settles to the bottom. The temporary dispersion of sand in water is called a *suspension*. By allowing the water to pass through a filter paper, one can trap the sand. The mixture is obviously heterogeneous, for part of it is clearly sand with one set of properties and part of it is water with another set of properties.

Is there nothing in between the true solution, with particles the size of ordinary molecules and ions, and suspensions with gross chunks of insoluble matter? Yes, there is something else. And it is a highly important arrangement of matter at that—the *colloidal state*.

Colloids are defined not by the kind of matter they contain but by the *size of the particles* involved. True solutions have particles of about 0.05 to about 0.25 nanometres (nm) in diameter (1 nm = 10^{-9} m). Suspensions have particles with diameters of 100 nm or more. Particles intermediate between these are said to be colloidal.

The properties of a *colloidal dispersion* are different from those of a true solution and also different from those of a suspension (**table 9.2**). Colloidal particles cannot be filtered by filter paper, nor do they settle on standing. Colloidal dispersions usually appear milky or cloudy. Even those that appear clear will reveal a beam of light which passes through the dispersion (**figure 9.13**). This phenomenon, called the *Tyndall effect*, is not observed in true

Table 9.2
Properties of solutions, colloids, and suspensions

Property	*Solution*	*Colloid*	*Suspension*
Particle size	0.1–1.0 nm	1–100 nm	>100 nm
Settles on standing?	No	No	Yes
Filter with paper?	No	No	Yes
Separate by dialysis?	No	Yes	Yes
Homogeneous?	Yes	Borderline	No

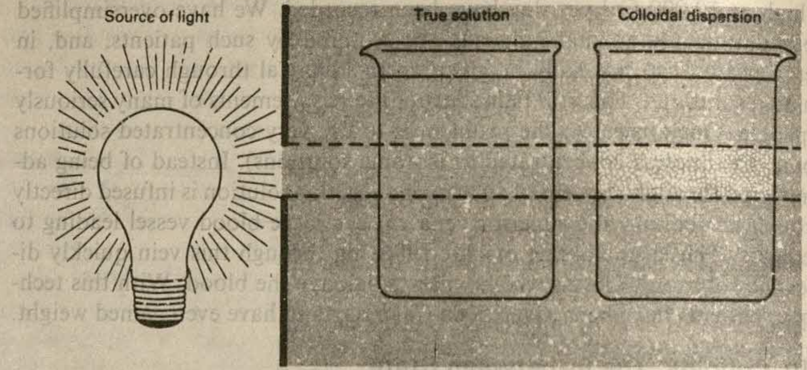


Figure 9.13 A beam of light passes through a true solution without noticeable effect. The same beam, passing through a colloidal solution, is clearly visible, because the light is scatted by the colloidal particles. This phenomenon is called the Tyndall effect.

solutions. Colloidal particles, unlike tiny molecules, are large enough to scatter and reflect light off to the side. You have probably observed the Tyndall effect in a movie theater. The shaft of light which originates in the projection booth and ends at the movie screen is brought to you through the courtesy of colloidal dust particles in the air.

There are eight different kinds of colloids, based on the physical state of the particles themselves (the dispersed phase) and that of the "solvent" (the dispersing phase). These are listed, with examples of each, in **table 9.3.**

The most important colloids in biological systems are emulsions—either liquids or solids dispersed in water. Protoplasm consists of colloidal particles as well as simple ions and molecules. Substances with high formula weights, such as starches and proteins, often form colloidal dispersions rather than true solutions in water.

In most colloidal dispersions, the particles are charged. This charge is often due to the adsorption of ions on the surface of a particle. A given colloid will preferentially adsorb only one kind of ion (either positive or

Table 9.3
Types of colloidal suspensions

Type	*Particle Phase*	*Medium Phase*	*Example*
Foam	Gas	Liquid†	Whipped cream
Solid foam	Gas	Solid	Floating soap
Aerosol	Liquid	Gas	Fog, hair sprays
Liquid emulsion	Liquid	Liquid	Milk, mayonnaise
Solid emulsion	Liquid	Solid	Butter
Smoke	Solid	Gas	Fine dust or soot in air
Sol*	Solid	Liquid	Starch solutions, jellies
Solid sol	Solid	Solid	Pearl

*Sols which set up in semisolid, jellylike form are called gels.

†By their very nature, gas mixtures always qualify as solutions. The size of particles in gas mixtures and their homogeneity fulfill the requirements of solutions.

negative) on its surfaces; thus, all the particles of a given colloidal dispersion bear like charges. Since like charges repel, the particles tend to stay away from one another. They cannot come together and form particles large enough to settle out. These colloids can be made to coalesce and separate out by addition of ions of opposite charge, particularly those doubly or triply charged. Aluminum chloride ($AlCl_3$), which contains Al^{3+} ions, is great for breaking up colloids in which the particles are negatively charged.

Other colloids are stabilized by addition of a material which provides a protective coating. Oil is ordinarily insoluble in water, but it can be emulsified by soap. The soap molecules form a negatively charged layer about the surface of each tiny oil droplet. These negative charges keep the oil particles from coming together and separating out. In a similar manner, bile salts emulsify the fats we eat, keeping them dispersed as tiny particles which can be more efficiently digested. Milk is an emulsion in which fat droplets are stabilized by a coating of casein, a protein. Casein, soap, and bile salts are examples of *emulsifying agents*, substances which stabilize emulsions.

9.11 Dialysis: The Ins and Outs of Life

In order to live, an organism must take in food and get rid of toxic wastes. The nutrients necessary to life must be gotten into cells, and the wastes must be gotten out. Generally, then, cell membranes must permit the passage not only of water molecules but also of other small molecules and ions. At the same time, it is important that large molecules and colloidal particles not be lost from the cell. Membranes that pass small molecules and ions while holding back large molecules and colloidal particles are called *dialyzing membranes*. The process is called *dialysis*. It differs from osmosis in that osmotic membranes pass only solvent molecules.

Laboratory use is made of dialyzing membranes to purify colloidal dispersions of smaller molecules and ions. The mixture to be purified is placed in a bag made of a dialyzing membrane. The bag is placed in a container of pure water (**figure 9.14**). The ions and small molecules pass out through the membrane, leaving the colloidal particles behind. Pure water is continually pumped past the bag, and the unwanted small particles are carried away.

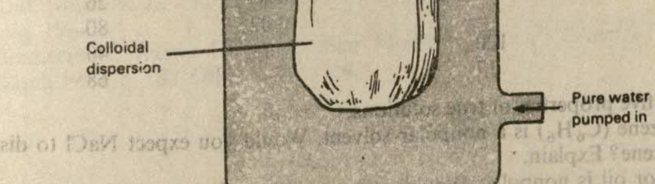


Figure 9.14 A simple apparatus for dialysis.

The dialyzing membrane may be an animal bladder or it may be an artifical one made from cellophane or from collodian, a semisynthetic plastic made by treatment of cellulose with nitric acid, alcohol, and camphor.

The kidneys are a complex dialyzing system responsible for the removal of certain potentially toxic waste products from the blood. By first gaining an understanding of the function of living kidneys, scientists have been able to construct artificial ones. Artificial kidneys are more elaborate in structure than the simple apparatus shown in **figure 9.14,** but their principle of operation is the same. We will discuss the operation of kidneys, both living and artificial, in chapter 28.

Many substances—medications, poisons, anesthetics—are thought to act by changing the permeability of membranes. Methyl mercury, a powerful poison which acts on the nervous system, is thought to act by making the membranes of nerve cells leakier than normal. A person going into shock has leaky capillaries which allow proteins and other colloidal particles as well as fluids to escape into the spaces between cells. If untreated, the cells may die from lack of oxygen and nutrients. As research increases our understanding of cellular membranes, we will undoubtedly gain a better understanding of drug action and of poisoning, of health and of disease.

Problems

1. Define and, where possible, illustrate these terms
   a. solution
   b. solvent
   c. solute
   d. miscible
   e. immiscible
   f. saturated
   g. unsaturated
   h. supersaturated
   i. soluble
   j. insoluble
   k. percent by volume
   l. percent by weight
   m. molarity
   n. dilute
   o. concentrated
   p. milligram percent
   q. ppm
   r. ppb
2. Without referring to **table 9.1,** indicate which compounds you would expect to be soluble in water. Explain each answer. You may use a periodic table.
   a. CH_3CH_2OH
   b. CH_3CH_2Cl
   c. $CH_3CH_2NH_2$
   d. CH_2O
   e. CCl_4
   f. CS_2
   g. $C_{12}H_{22}O_{11}$
   h. NaBr
   i. $(NH_4)_2CO$
   j. $Ca(NO_3)_2$
   k. RbCl
   l. $BaCO_3$
   m. $SrSO_4$
   n. $C_{10}H_{20}O$
3. Complete the following table.

Concentration of Solute (in grams per litre)	*Molarity*	*Formula Weight of Solute*
98	1.0	—
32	0.5	—
0.74	0.01	—
—	0.1	26
—	0.025	80
120	—	40
17	—	68

4. List five properties of true solutions.
5. Benzene (C_6H_6) is a nonpolar solvent. Would you expect NaCl to dissolve in benzene? Explain.
6. Motor oil is nonpolar. Would you expect it to dissolve in water? In benzene? Explain.

7. Bubbles of carbon dioxide escape when the cap is removed from a bottle of pop. Explain.
8. What is the freezing point of 1 kg of water which has 1 mole of urea (NH_2CONH_2) dissolved in it? What is the boiling point of the solution? What would be the boiling point if 2 moles of urea were dissolved in 1 kg of water?
9. You have a stock solution of 6 *M* HCl. How many moles of HCl are there in 1.0 ℓ? In 100 ml? In 1 ml?
10. On the average, glucose ($C_6H_{12}O_6$) makes up about 0.10% by weight of human blood. How much glucose is there in 1 kg of blood?
11. Tell exactly how you would prepare each of these solutions. In each case, state exactly how much solute you would weigh out and how much solvent you would use or how much solution you would make.
    a. about 100 ml of a 5%-by-weight NaOH solution
    b. exactly 1 ℓ of 2 *M* NaCl solution
    c. exactly 500 ml of a 0.5 *M* $C_6H_{12}O_6$ solution
    d. about 1 ℓ of a 10%-by-weight $NaHCO_3$ solution
    e. about 500 ml of a 0.92%-by-weight NaCl solution
12. Compare and contrast true solutions, colloidal dispersions, and suspensions.
13. Define and, where possible, illustrate these terms.
    a. osmosis
    b. semipermeable membrane
    c. dialyzing membrane
    d. hypotonic solution
    e. hypertonic solution
    f. isotonic solution
    g. plasmolysis
    h. hemolysis
    i. dialysis
    j. crenation
    k. BOD
    l. hydrate
    m. anhydrous compound
    n. hygroscopic compound
    o. efflorescent compound
    p. deliquescent compound
14. Compare and contrast osmosis and dialysis with regard to the kind of particles that pass through the membrane.
15. Which will give the more concentrated solution—a dilution of 1:20 or a dilution of 1:2000?

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chapter 10

Acids and Bases

Ours is a strange, sometimes perplexing, yet wondrous world. All of us practice a complicated chemistry, from the baking of bread to the treatment of heartburn and headache and beyond. Central to much of the chemistry that we practice are two special kinds of compounds called acids and bases. We use lots of acids and bases around the home (**figure 10.1**). We use them for cleaning. We eat them and drink them. Our bodies produce them and consume them.

The quantitative aspects of acid-base chemistry will be discussed in chapter 11. In this chapter we will look at some of the more qualitative properties of acids and bases—what they are, how they are produced, how they are named, and how they react chemically.

10.1 Acids and Svante Arrhenius

Acidic substances have been known for millennia. However, it was only in 1887 that Svante Arrhenius, a young Swedish chemist still in graduate school, proposed definitions of acids and bases that are still in common use today. Acids were generally recognized as substances which, in aqueous solution, would:

1. Turn the "indicator" dye litmus from blue to red.
2. React with active metals such as zinc, iron, and tin, dissolving the metal and producing hydrogen gas.
3. Taste sour, if diluted enough to be safely tasted.
4. React with certain compounds called alkalis or bases to form water and compounds called salts.

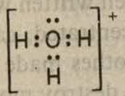
Arrhenius proposed that these characteristic properties of acids are actually properties of the hydrogen ion (H^+) and that acids are compounds which yield hydrogen ions in aqueous solutions.

Arrhenius' definition is still useful—as long as we deal only with aqueous solutions. If you want to know whether or not a given compound is an

Arrhenius acid, just dissolve some of it in water. Stick in a piece of blue litmus paper. If the litmus turns red, the compound is an acid.

Many foods are acidic. Vinegar contains 4% to 10% acetic acid. Citrus fruits—and many fruit-flavored drinks—contain citric acid. If a food tastes sour, it most likely contains one or more acids.

Arrhenius' theory has been modified somewhat through the years. We know, for example, that simple hydrogen ions do not exist in water solutions. When a hydrogen atom is stripped of its only electron, all that is left is the bare nucleus containing a single proton. Other positive ions, even the relatively small lithium ion (Li^+), still have their nuclei shielded by electrons remaining in the inner shells. Thus, the hydrogen ion (also referred to as a proton) is too reactive to exist as a stable ion in solution. We know today that the acidic properties of a solution are due to H_3O^+, in which each hydrogen atom shares a pair of electrons with oxygen. The electronic configuration is



$$\left[\begin{array}{c} \mathrm{H:\ddot{O}:H} \\ \mathrm{\overset{\bullet\bullet}{H}} \end{array}\right]^+$$

This species is called the *hydronium ion*. Today, we might well say that an acid is a substance which produces hydronium ions when dissolved in water. Even the hydronium ion is an oversimplification, for it is hydrated by other water molecules. For most purposes, though, we can use the simple hydronium ion (H_3O^+) and ignore any further hydration. The situation is not as bad as it may seem. The hydronium ion is quite reactive; it can readily transfer a proton to other molecules and ions. Thus, to talk about protons when we mean their source (hydronium ions) is permissible as long as we understand that we are using a simplification of the real situation.

Some acids give up one hydrogen ion (proton) per molecule. These are called *monoprotic acids*. An example is hydrogen chloride. When this compound, a gas, is dissolved in water, we get one hydronium ion per molecule of hydrogen chloride.

$$HCl(g) + H_2O \longrightarrow H_3O^+(aq) + Cl^-(aq)$$

(The symbol *g* in parentheses indicates the gaseous state; *aq* in parentheses indicates an aqueous solution.)

Other acids may give up more than one hydrogen ion per molecule. Sulfuric acid (H_2SO_4) is a *diprotic acid*, for it is capable of giving up two protons. Similarly phosphoric acid (H_3PO_4) is a *triprotic acid*. A general term for acids which give up more than one proton is *polyprotic*. You should not assume that all the hydrogen atoms in a compound are acidic, meaning that they are released in water solutions. For example, none of the hydrogens of methane (CH_4) is given up in aqueous solution. Only one of the hydrogens in acetic acid ($C_2H_4O_2$) is acidic. For this reason, the formula for acetic acid is frequently written CH_3COOH or $HC_2H_3O_2$ to emphasize that only one proton is released. You will gain experience in determining

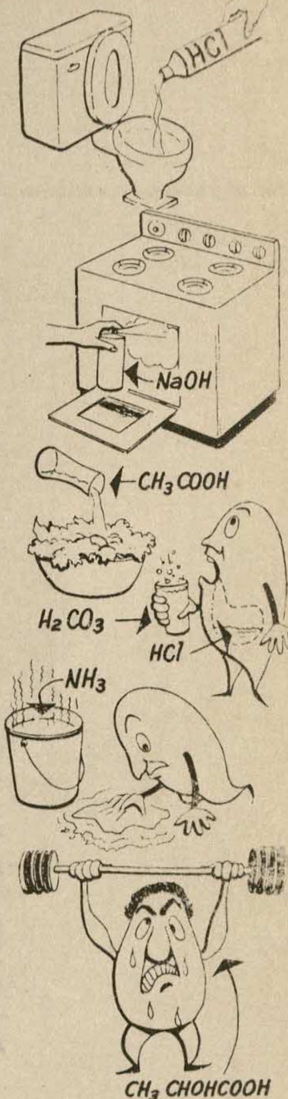


Figure 10.1 Some uses and occurrences of acids and bases

which hydrogen atoms in a molecule are acidic as you learn more about molecular structure.

10.2 Strong Acids, Weak Acids

Strong acids are those which ionize completely (each molecule in dilute solution donates its acidic protons to water). Acids which ionize nearly completely are also called strong acids. In an equation, the ionization of a strong acid is sometimes shown as an equilibrium between un-ionized and ionized forms.

$$HCl + H_2O \rightleftharpoons H_3O^+ + Cl^-$$

The unequal double arrow indicates that the equilibrium strongly favors the ionized form. Because strong acids are essentially completely ionized in solution, the equation is most often written with a single arrow.

Strong acids, if fairly concentrated, can cause serious damage to skin and flesh. They eat holes in clothes made of natural fibers such as cotton, silk, or wool. Strong acids also destroy most synthetics such as nylon, polyester, and acrylic fibers. Care should always be taken to prevent spills on either skin or clothing. In very dilute solutions, acids may well prove harmless. Hydrochloric acid, for example, is produced in dilute solution in our stomachs, where it aids in the digestion of certain foodstuffs. (Even here, under certain conditions, it can cause problems—as anyone with an ulcer can attest.)

Acids which ionize only slightly in dilute solution are called *weak acids*. Acetic acid (CH_3COOH) is an example. The equation for the ionization of this acid is drawn in such a way as to indicate a preference for the un-ionized form.

$$CH_3COOH + H_2O \rightleftharpoons CH_3COO^- + H_3O^+$$

Solutions of 4% to 10% acetic acid are called vinegar, a familiar condiment. We should be aware, though, that while it is safe to eat (oil and) vinegar on

Table 10.1
Some representative acids

Name	*Formula*	*Classification*	*Number of Hydronium Ions from 1 000 000 Molecules in 0.01* M *Solution*
Sulfuric acid	H_2SO_4	Strong	1 220 000
Nitric acid	HNO_3	Strong	920 000
Hydrochloric acid	HCl	Strong	920 000
Phosphoric acid	H_3PO_4	Moderate	270 000
Lactic acid	$CH_3CHOHCOOH$	Weak	87 000
Acetic acid	CH_3COOH	Weak	13 000
Boric acid	H_3BO_3	Weak	Less than 1
Hydrocyanic acid	HCN	Weak	Less than 1

our salad, more concentrated acetic acid solutions can be corrosive to the skin and especially so to the digestive tract.

A sampling of strong and weak acids is given in **table 10.1.** Many of them will be encountered again and again as we continue our study of chemistry.

10.3 Acids: The Naming Game

In chapter 4 you learned the names of some common anions (and if you didn't—now is the time). It is easy to learn the names of acids derived from these anions. Just follow these simple rules.

If the anion name ends in *-ide, -ate,* or *-ite,* then the acid name is, respectively, hydro____ic acid, ____ic acid, or ____ous acid. Let's apply these rules to a few examples.

Ion	*Name*	*Acid*	*Name*
Cl^-	Chloride	HCl	Hydrochloric acid
NO_3^-	Nitrate	HNO_3	Nitric acid
SO_4^{2-}	Sulfate	H_2SO_4	Sulfuric acid
PO_4^{3-}	Phosphate	H_3PO_4	Phosphoric acid
SO_3^{2-}	Sulfite	H_2SO_3	Sulfurous acid
CO_3^{2-}	Carbonate	H_2CO_3	Carbonic acid
CN^-	Cyanide	HCN	Hydrocyanic acid
S^{2-}	Sulfide	H_2S	Hydrosulfuric acid
CH_3COO^-	Acetate	CH_3COOH	Acetic acid
BO_3^{3-}	Borate	H_3BO_3	Boric acid

Note that most of the names have the same stem in the acid as in the anion. A few have extra letters; for example, the *ur* in sulfuric and sulfurous, and the *or* in phosphoric. These you will have to learn as special cases if you haven't done so already.

Any acid with three or more replaceable hydrogens can exist in two forms, called *ortho* and *meta*. The meta form can be derived by subtracting two hydrogens and one oxygen (i.e., H_2O) from the ortho formula. For example, H_3PO_4 is really orthophosphoric acid, although the prefix is often dropped in everyday usage. Metaphosphoric acid is therefore HPO_3 (i.e., H_3PO_4 minus H_2O). Metaboric acid is derived in a similar manner from orthoboric acid (H_3BO_3). Subtraction of H_2O gives HBO_2. The corresponding anions are metaphosphate (PO_3^-) and metaborate (BO_2^-). Sodium metaphosphate and sodium metasilicate are used as water softeners.

Example 10.1 The formula for phosphite ion is PO_3^{3-}. What is the formula for (ortho) phosphorous acid? For metaphosphorous acid? For metaphosphite ion?

Orthophosphorous acid is H_3PO_3 (add one H^+ for each negative charge on PO_3^{3-}). Metaphosphorous acid is HPO_2 (H_3PO_3 minus H_2O). The metaphosphite ion is PO_2^-.

We will encounter other acids as we go along. The names of most will be obvious from the preceding discussion. A few will have special, nonsystematic names. The names of important organic acids (of which acetic and lactic acid are but two examples) will be given in chapter 18.

10.4 Touching a Few Bases

Like acids, basic compounds have been known for thousands of years. According to the biblical account, the Israelites, in their journey from Egypt to Palestine, came upon bitter waters at Marah (Exod. 15:23). Although the writers may not have meant to, they thus recorded for posterity the existence of an aqueous solution of base. By the time of Arrhenius, bases, or alkaline compounds, were generally recognized as those substances which, when dissolved in water, would:

1. Turn the indicator dye litmus from red to blue.
2. Feel slippery or soapy on the skin.
3. Taste bitter (as the Israelites found at Marah).
4. React with acids to form water and salts.

Arrhenius' theory was that these were actually properties of the hydroxide ion (OH^-). Bases, he said, are compounds that yield *hydroxide ions* in aqueous solutions.

Perhaps the most familiar strong base is sodium hydroxide (NaOH), sometimes called lye. Even in the solid state, sodium hydroxide is completely ionic; that is, it exists as sodium ions and hydroxide ions. In solution, the hydroxide ions enter into the characteristic reactions which we refer to when we say a solution is basic.

Other common bases are potassium hydroxide (KOH), calcium hydroxide [$Ca(OH)_2$], and magnesium hydroxide [$Mg(OH)_2$]. All of these are completely ionic, yet only potassium hydroxide is classified as a strong base. Potassium hydroxide, like sodium hydroxide, is very soluble in water. Therefore, aqueous solutions of the compound are rich in hydroxide ions. Calcium hydroxide is only sparingly soluble in water; the solution thus contains relatively little dissolved hydroxide ion and is not strongly basic. Magnesium hydroxide is so nearly insoluble that it can be safely taken internally as an antacid (section 10.8).

Ammonia (NH_3) is a familiar weak base. It is a gas at room temperature but readily dissolves in water to give a basic solution. It reacts with water to a slight extent to produce ammonium ions (NH_4^+) and hydroxide ions.

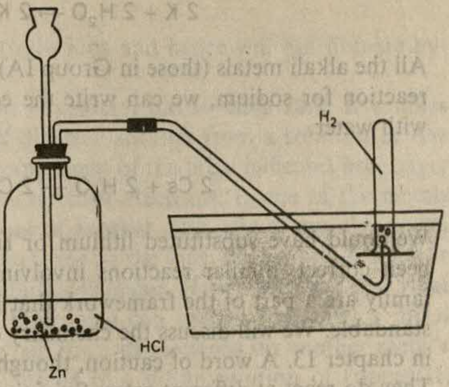
$$NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^-$$

Ammonia is called a weak base for the same reason that magnesium and calcium hydroxide are. The solution of ammonia contains a relatively low concentration of hydroxide ions. In the case of ammonia, however, it is not that ammonia is insoluble but rather that once ammonia is in solution it tends *not* to ionize. The solution so formed is sometimes called *ammonium hydroxide*, but since most of the nitrogen atoms are still in the form of NH_3, *aqueous ammonia* is perhaps a better name. Many familiar household cleansers contain ammonia, a compound easily detected by its characteristic odor.

10.5 Acids, Metals, and the Activity Series

We have repeatedly said that acids and bases have characteristic reactions. One such reaction for acids is that with certain metals. For example,

Figure 10.2 Zinc reacts with hydrochloric acid to produce hydrogen gas. The hydrogen can be collected by displacement of water from a test tube inverted in a pan of water.



if zinc metal is treated with hydrochloric acid, hydrogen gas is produced along with a salt, zinc chloride (**figure 10.2**). The equation may be written

$$Zn(s) + 2\ HCl(aq) \longrightarrow ZnCl_2(aq) + H_2(g)$$

Since zinc chloride is ionic and hydrogen chloride ionizes in aqueous solution, the equation may also be written

$$Zn(s) + 2\ H_3O^+ + 2\ Cl^- \longrightarrow Zn^{2+} + 2\ Cl^- + H_2(g) + 2\ H_2O$$

In this form, the equation clearly indicates that the chloride ions are not really involved in the reaction. They appear as reactants and, unchanged, as products. We can eliminate them from the equation and still accurately record the changes that have occurred. The *net* ionic equation becomes

$$Zn + 2\ H_3O^+ \longrightarrow Zn^{2+} + H_2(g) + 2\ H_2O$$

This equation tells us that zinc will react with *any* acid (i.e., any source of hydronium ions) to produce zinc ions and hydrogen gas. Both of the following equations can be reduced to a net ionic equation identical to the one shown above.

$$Zn(s) + H_2SO_4(aq) \longrightarrow ZnSO_4(aq) + H_2(g)$$
$$Zn(s) + 2\ HNO_3(aq) \longrightarrow Zn(NO_3)_2(aq) + H_2(g)$$

Zinc is one of a number of "active" metals which react with acids in this way. Not all these metals react at the same rate, however. Some, such as sodium and potassium, react violently with plain water—without any added acid. The reaction may produce enough heat to ignite the hydrogen gas, causing an explosion. With sodium, the by-product is a solution of sodium hydroxide.

$$2\ Na + 2\ H_2O \longrightarrow 2\ NaOH(aq) + H_2$$

A similar reaction occurs with potassium.

$$2\ K + 2\ H_2O \longrightarrow 2\ KOH(aq) + H_2$$

All the alkali metals (those in Group IA) react in this manner. Knowing the reaction for sodium, we can write the equation for the reaction of cesium with water.

$$2\ Cs + 2\ H_2O \longrightarrow 2\ CsOH(aq) + H_2$$

We could have substituted lithium or rubidium for cesium and still have been correct. Similar reactions involving members of the same chemical family are a part of the framework that helps make chemistry more understandable. We will discuss the chemistry of some of the families of elements in chapter 13. A word of caution, though. Even members of a family differ. They do react at different rates. Sometimes even the *kind* of reaction is different. But these exceptions will not concern us very much here.

In contrast to the alkali metals, metals like zinc or iron do not react appreciably when placed in water. However, if the temperature is raised and zinc is brought into contact with steam, then hydrogen gas is produced. Tin won't react with steam, but it will release hydrogen on contact with acids. Gold won't even react with acids.

It is possible to arrange metals in an *activity series* with the most reactive metals (such as potassium) at the top and the least reactive (such as gold) at the bottom (**table 10.2**). The position of a metal in the table reflects its tendency to give up electrons to form ions. All of those listed above hydrogen in the series (the "active" metals) will react with acids to produce hydrogen gas. In order to become ions, these metals will force their electrons on the hydrogen ions produced by the acids. Those metals below hydrogen

Table 10.2
An activity series of the metals

Potassium	React with cold water, releasing hydrogen
Calcium	
Sodium	
Magnesium	React with steam, releasing hydrogen
Aluminum	
Zinc	
Chromium	
Iron	
Nickel	React with acids, releasing hydrogen
Tin	
Lead	
Hydrogen	
Copper	Do not react with acids to form hydrogen
Silver	
Mercury	
Platinum	
Gold	

will not give up electrons to hydrogen ions and hence will not liberate hydrogen gas from acids.

A lot of chemical information is summarized in **table 10.2.** It enables one to predict which element will displace another from a solution of one of its salts. Remember that the arrangement of the table indicates how eager these metallic elements are to give up their electrons. If one of the metals is brought into contact with the ions of another, then one of two things can happen. The metal will force its electrons on the ions, or the ions will refuse to accept the electrons and no reaction will occur. How does one know what will actually happen? Using the table, one can predict that only a metal which appears higher in the table can force its electrons on another metal's ions. For example, an iron nail, placed in a dilute solution of copper(II) sulfate ($CuSO_4$), gradually becomes coated with copper metal (**figure 10.3**). Since iron atoms have a greater tendency to give up electrons than do copper atoms, the iron atoms transfer electrons to the copper ions.

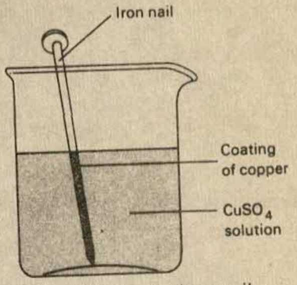


Figure 10.3 An iron nail placed in a solution of copper sulfate becomes coated with copper.

$$Fe + Cu^{2+} \longrightarrow Fe^{2+} + Cu$$

What we observe is the copper metal plating out of solution as it is formed. Some of the iron dissolves as iron(II) ions, but this is not as obvious to the observer.

If one uses another system, it is possible to see both processes as they occur. A strip of copper metal placed in a solution of silver nitrate ($AgNO_3$) becomes coated with crystals of metallic silver (**figure 10.4**). The silver ions grab electrons from the more reactive copper atoms.

$$2\ Ag^+ + Cu \longrightarrow 2\ Ag + Cu^{2+}$$

There is also visual evidence that the copper is dissolving. A solution of copper ions is blue, whereas a solution of silver ions is colorless. Thus, as the silver metal crystallizes out of solution, the copper ions form and slowly turn the solution blue.

Note that in one of the examples copper loses electrons and in the other it gains them. That is because there are elements both above and below copper in the activity series, and what happens depends only on the *relative* reactivity of the elements involved.

Figure 10.4 A chemical tree made from copper wire and a silver nitrate solution. Copper ions replace silver ions in solution. (Reprinted with permission from Toler, Richard J., "A Chemical Christmas Tree," *Chemistry*, December 1974. Copyright © 1974 by the American Chemical Society.)

10.6 Neutralization: Back to the Acid, Base, and Salt Mines

As a characteristic property of both acids and bases, we listed the reaction of these compounds with one another to form water and a salt. Sodium hydroxide reacts with hydrochloric acid to produce water and sodium chloride, a salt (in this case, ordinary table salt).

$$NaOH(aq) + HCl(aq) \longrightarrow H_2O + NaCl(aq)$$

If equivalent amounts of acid and base (e.g., 100 ml each of 0.1 *M* solution) are used, the resulting solution no longer affects litmus paper. Nor does the new solution taste bitter or sour; it tastes salty. The solution is neither acidic nor basic. It is neutral, and the reaction is called *neutralization*.

Both aqueous sodium hydroxide and aqueous hydrogen chloride are ionic. The solution formed by mixing of the two contains sodium chloride, which is also ionic. Rewriting the equation in ionic form, we get

$$Na^+ + OH^- + H_3O^+ + Cl^- \longrightarrow 2\ H_2O + Na^+ + Cl^-$$

In a similar manner we can write the equation for the reaction of potassium hydroxide with nitric acid.

$$KOH(aq) + HNO_3(aq) \longrightarrow H_2O + KNO_3(aq)$$

Cr

$$K^+ + OH^- + H_3O^+ + NO_3^- \longrightarrow 2\ H_2O + K^+ + NO_3^-$$

Note that in each reaction hydrogen ions come together with hydroxide ions to form water. The other ions are left unchanged in the solution. Thus, for any neutralization, we can write the *net* ionic reaction as

$$H_3O^+ + OH^- \longrightarrow 2\ H_2O$$

The other ions don't just disappear. If the solution after neutralization is evaporated, a crystalline ionic solid—a *salt*—is obtained. In general, then, we can say that an acid reacts with a base to form a salt and water.

10.7 Here Comes the Fizz: Reactions of Acids with Carbonates and Bicarbonates

Add vinegar to baking soda and you get a vigorous fizzing action. Some antacid preparations are designed to effervesce. What causes the fizz? Generally, it is the reaction of a carbonate or bicarbonate salt with an acid.

Carbonates and bicarbonates are salts of carbonic acid (H_2CO_3). This diprotic acid is a very weak one; it holds on to its protons quite tightly. (Notice the apparent contradiction: it's the weak acids that hold tightly to their protons and the strong acids that don't.) Conversely, carbonate ions and bicarbonate ions pick up protons readily to form carbonic acid. Further, carbonic acid is quite unstable. It decomposes to carbon dioxide and water.

$$H_2CO_3(aq) \longrightarrow H_2O + CO_2(g)$$

This reaction is not related to the acidity of carbonic acid. It simply indicates that the compound, which happens to be an acid, is not stable. One can't purchase a bottle of carbonic acid; it is too unstable to be isolated and bottled. It can, however, be formed in solution. But as soon as it is formed, it tends to decompose.

If sodium bicarbonate is dissolved in water, a solution of sodium ions and bicarbonate ions is formed. If hydrochloric acid is added, the bicarbonate ions come into contact with the hydronium ions from the acid and immediately grab a proton to form carbonic acid.

$$Na^+ + HCO_3^- + H_3O^+ + Cl^- \longrightarrow H_2CO_3 + Na^+ + Cl^- + H_2O$$

But carbonic acid is unstable and immediately falls apart, forming carbon dioxide and water. The gaseous carbon dioxide bubbles out of solution (the fizz). If the remaining solution is evaporated, sodium chloride is left. Even if acid is poured on solid sodium bicarbonate, carbon dioxide is released. The reaction may be written

$$NaHCO_3\,(s\text{ or }aq) + HCl(aq) \longrightarrow NaCl(aq) + CO_2(g) + H_2O$$

The net ionic equation is simpler.

$$HCO_3^- + H_3O^+ \longrightarrow \underset{\begin{array}{c}+\\ H_2O\end{array}}{H_2CO_3} \longrightarrow H_2O + CO_2$$

Similarly, if hydrochloric acid is added to sodium carbonate, bubbles of carbon dioxide and a solution of sodium chloride are formed.

$$Na_2CO_3\,(s\text{ or }aq) + 2\,HCl(aq) \longrightarrow 2\,NaCl(aq) + CO_2(g) + H_2O$$

The net ionic equation shows that the doubly negative carbonate ion picks up two protons to form carbonic acid. The latter breaks down to form carbon dioxide and water.

$$CO_3^{2-} + 2\,H_3O^+ \longrightarrow \underset{\begin{array}{c}+\\ 2\,H_2O\end{array}}{H_2CO_3} \longrightarrow H_2O + CO_2$$

Limestone and marble are mainly calcium carbonate ($CaCO_3$). Both are important building stones. Marble is also used in statues, monuments, and sculptures. The calcium carbonate in them is readily attacked by acids in the atmosphere or in rain. And the atmosphere has been made increasingly acidic in recent years, mainly by the burning of sulfur-containing coal. The sulfur combines with oxygen to form sulfur dioxide.

$$S + O_2 \longrightarrow SO_2$$

Some of the sulfur dioxide reacts further with oxygen to form sulfur trioxide.

$$2\,SO_2 + O_2 \longrightarrow 2\,SO_3$$

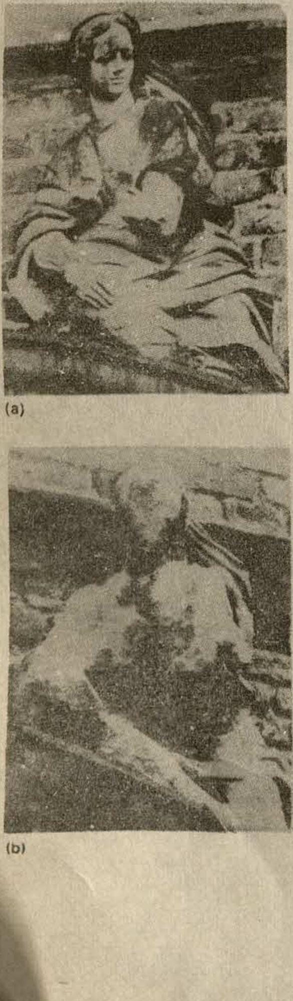
The sulfur trioxide then reacts with water to form sulfuric acid.

$$SO_3 + H_2O \longrightarrow H_2SO_4$$

The sulfuric acid, in the form of an aerosol mist or diluted by rainwater, furnishes the hydronium ions which dissolve the marble and limestone.

$$CaCO_3(s) + 2\,H_3O^+ \longrightarrow Ca^{2+}(aq) + CO_2(g) + 3\,H_2O$$

Figure 10.5 This stone sculpture on the exterior of Herten Castle, near Recklinghausen, in Westphalia, Germany, shows the effects of acidic smog. The castle was constructed in 1702. (a) The sculpture as it looked in 1908. (b) The sculpture as it looked in 1969. (Reprinted with permission from Winkler, E. M., *Stone: Properties, Durability in Man's Environment,* Berlin: Springer-Verlag, 1973. Copyright © 1973 by E. M. Winkler.)



The acid mists and acidic rainwater also attack and dissolve many metals (section 10.5). Damage to our buildings, automobiles, and other structures and machines from air pollution amounts to billions of dollars per year. And even then the story is not complete. These acid pollutants are also damaging to crops and to human health, as we shall see in section 10.10.

10.8 An Acid-Base Laboratory: Your Stomach

The stomach secretes hydrochloric acid (HCl) as an aid in the digestion of food. Sometimes overindulgence or emotional stress leads to a condition called hyperacidity (too much acid). A number of antacids are available to treat this condition, many of them aggressively advertised. Indeed, sales of antacids in the United States were estimated to be $117 million in 1972. Let's look at some popular antacids from the standpoint of acid-base chemistry.

Tums, a familiar antacid tablet, contains calcium carbonate ($CaCO_3$), magnesium carbonate ($MgCO_3$), and magnesium trisilicate ($Mg_2Si_3O_8$). Calcium carbonate, an effective antacid, is also an antidiarrheal. Magnesium carbonate, used as an antacid in small doses, is an effective laxative in larger doses. Magnesium trisilicate is used in the treatment of ulcers and gastritis.

Rolaids, often boasted of as consuming 47 times its weight in "stomach acid," has aluminum sodium dihydroxy carbonate [$AlNa(OH)_2CO_3$] as the only active ingredient. (See reference 4 for an interesting investigation of this claim.) Both the hydroxide ion (OH^-) and the carbonate ion (CO_3^{2-}) consume acid (H_3O^+ ions).

$$OH^- + H_3O^+ \longrightarrow 2\ H_2O$$

$$CO_3^{2-} + 2\ H_3O^+ \longrightarrow CO_2 + 3\ H_2O$$

Maalox, in the form of an aqueous suspension, contains magnesium hydroxide [$Mg(OH)_2$] and aluminum hydroxide [$Al(OH)_3$]. The former is an antacid and a laxative; the latter is an antacid and is antidiarrheal. How's that for balance?

Alka-Seltzer, often recommended for overindulgence or upset stomach, contains calcium dihydrogen phosphate [$Ca(H_2PO_4)_2$], sodium bicarbonate ($NaHCO_3$), citric acid (chapter 18), and aspirin. The familiar fizz is due to the carbon dioxide gas released by the reaction of bicarbonate ions with the acidic components when dissolved.

$$HCO_3^- + H_3O^+ \longrightarrow CO_2 + 2\ H_2O$$

Alka-Seltzer came under attack because the aspirin might be harmful to people with ulcers and other stomach disorders. To offset that criticism, the makers introduced *Alka-Seltzer Gold,* which does not contain aspirin.

Probably the cheapest and most effective antacid is calcium carbonate ($CaCO_3$), commonly called precipitated chalk. The compound, however, causes constipation in some people. There is also recent evidence that calcium ions (Ca^{2+}) actually trigger the release of *more* hydrochloric acid, leading to an "acid rebound" worse than the original hyperacidity.

Milk of magnesia, a suspension of magnesium hydroxide [$Mg(OH)_2$] in water, serves as a laxative in large dosages and as an antacid at lower dose levels. It is sold under a variety of trade names. Sodium bicarbonate, or baking soda ($NaHCO_3$), is safe for occasional use. Overuse may make the blood too alkaline, a condition called alkalosis.

Other indigestion remedies contain still other drugs. *Bromo Seltzer* once contained, among other things, potassium bromide (KBr). According to *The Merck Index* (reference 10), large doses of potassium bromide cause depression of the central nervous system. Prolonged intake may cause mental deterioration and acneform skin eruptions. *Bromo Seltzer*, despite its name, no longer contains KBr. The current pain reliever in it is acetaminophen, an aspirin substitute (chapter 18). *Pepto-Bismol* is an antacid preparation which also contains an antidiarrheal drug. The main ingredient of any antacid preparation is a basic compound, that is, some compound which neutralizes acids. The acid-base chemistry of antacids is summarized in the following reactions.

$$CaCO_3 + 2\,HCl \longrightarrow CaCl_2 + H_2O + CO_2$$
$$MgCO_3 + 2\,HCl \longrightarrow MgCl_2 + H_2O + CO_2$$
$$MgO + 2\,HCl \longrightarrow MgCl_2 + H_2O$$
$$Mg(OH)_2 + 2\,HCl \longrightarrow MgCl_2 + 2\,H_2O$$
$$NaHCO_3 + HCl \longrightarrow NaCl + H_2O + CO_2$$

Antacid + stomach acid ⟶ a salt + water (+ carbon dioxide)

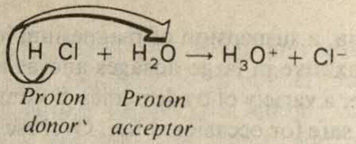
Notice that in each case the products are a compound of a metal and the nonmetal chlorine—a salt—and water. The carbonates and bicarbonates form carbon dioxide as an additional product. Since extra ingredients add little—except cost—to antacid preparations, you can choose your "base" on the basis of price.

Anyone with severe or repeated attacks of indigestion should consult a physician. Self-medication in such cases might be dangerous.

10.9 Protons, Anyone? The Brønsted-Lowry Theory

The Arrhenius theory of acids and bases was useful for many years. It is still useful today for many aqueous solutions. But by the 1920s chemists were working with solvents other than water. Compounds were found that acted like bases yet did not have OH in their formulas. A new theory was needed. One was suggested in 1923, at almost the same time, by J. N. Brønsted, a colleague of Neils Bohr (chapter 2) at Copenhagen, and by Thomas M. Lowry, of England.

The *Brønsted-Lowry theory* defines an *acid* as a *proton donor* (H^+ donor) and a *base* as a *proton acceptor* (H^+ acceptor). All the substances that Arrhenius considered acids are also acids by this definition. For instance, the reaction of hydrogen chloride with water has hydrogen chloride acting as a proton donor. All the Arrhenius bases are also bases in the new theory, but there are also new bases. In the hydrogen chloride–water reaction, the proton acceptor is water.



$$HCl + H_2O \longrightarrow H_3O^+ + Cl^-$$

Thus, water becomes a base in the Brønsted-Lowry system. The driving force for the reaction is the formation of a weaker acid (one which has less tendency to give up a proton) and a weaker base (one which has less tendency to accept a proton). A stronger acid reacts with a stronger base to produce a weaker base and a weaker acid.

$$\underset{\textit{Stronger acid}}{HCl} + \underset{\textit{Stronger base}}{H_2O} \longrightarrow \underset{\textit{Weaker acid}}{H_3O^+} + \underset{\textit{Weaker base}}{Cl^-}$$

It may not be obvious that hydrogen chloride is a stronger acid than hydronium ion, but keep in mind that a stronger acid is one that succeeds in giving away its proton. It is sort of the opposite of the "keep-away" game that children play; it's a "give-away" game. It may also seem odd to think of water as a base. Remember the definition, though. A base is a proton acceptor. Not only is water a base in that sense, but it is a stronger base than chloride ion. In the "give-away" game water gets the proton every time.

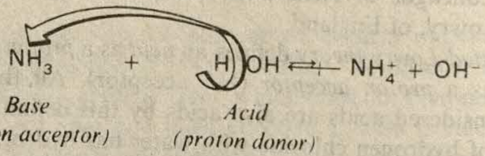
Hydrogen chloride and chloride ion make up a *conjugate* acid-base pair. Hydrogen chloride is an acid; chloride ion is its conjugate base (the conjugate base is the acid minus its proton). Water and the hydronium ion make up another conjugate pair. Water is a Brønsted-Lowry base; hydronium ion is its conjugate acid.

Conjugate acid-base pair

$$HCl + H_2O \longrightarrow H_3O^+ + Cl^-$$

Conjugate acid-base pair

Let's take another look at the aqueous ammonia system in terms of the Brønsted-Lowry theory. Ammonia reacts with water (to a slight extent) to form ammonium ions and hydroxide ions. In this system ammonia acts as a proton acceptor (base) and water acts as a proton donor (acid!).



$$NH_3 + HOH \rightleftharpoons NH_4^+ + OH^-$$

Ammonia and hydroxide ions compete for protons. Which is the stronger base? Hydroxide ion gets the proton most of the time. A dynamic equilibrium is established among all four species present. However, at any instant there are a lot more ammonia and water molecules than there are ammonium and hydroxide ions.

Ammonia and ammonium ion make up one conjugate pair, and water and hydroxide ion make up another.

Conjugate acid-base pair

$$\underset{\text{Weaker base}}{NH_3} + \underset{\text{Weaker acid}}{H_2O} \rightleftharpoons \underset{\text{Stronger acid}}{NH_4^+} + \underset{\text{Stronger base}}{OH^-}$$

Conjugate acid-base pair

Since the driving force is toward the weaker base and the weaker acid, it is easy to see that there would be more ammonia than ammonium ion and more water than hydroxide ion. Note that in such systems conjugate pairs always consist of a stronger and a weaker partner. This is certainly not a coincidence. What makes an acid stronger is its greater tendency not to hold its proton. It is necessarily true, therefore, that its conjugate base must not eagerly seek a proton and so is classified as weaker.

To summarize, a strong Brønsted-Lowry acid is one which readily gives up protons, and a weak acid is one which holds on to its protons tightly. A strong Brønsted-Lowry base is one which readily accepts protons and then binds them tightly. A weak base accepts a proton less readily and then holds it rather loosely. **Table 10.3** lists a number of acids and their conjugate bases in order of their relative strengths. Notice that the strongest acid has

Table 10.3

The relative strengths of some Brønsted-Lowry acids and their conjugate bases

Acid		*Base*	
Name	*Formula*	*Name*	*Formula*
Perchloric acid	$HClO_4$	Perchlorate ion	ClO_4^-
Sulfuric acid	H_2SO_4	Hydrogen sulfate ion	HSO_4^-
Hydrogen chloride	HCl	Chloride ion	Cl^-
Nitric acid	HNO_3	Nitrate ion	NO_3^-
Hydronium ion	H_3O^+	Water	H_2O
Sulfurous acid	H_2SO_3	Hydrogen sulfite ion	HSO_3^-
Phosphoric acid	H_3PO_4	Dihydrogen phosphate ion	$H_2PO_4^-$
Acetic acid	CH_3COOH	Acetate ion	CH_3COO^-
Carbonic acid	H_2CO_3	Hydrogen carbonate ion	HCO_3^-
Ammonium ion	NH_4^+	Ammonia	NH_3
Water	H_2O	Hydroxide ion	OH^-
Ammonia	NH_3	Amide ion	NH_2^-

Stronger acids ↑ Weaker acids ↓

Weaker bases ↑ Stronger bases ↓

the weakest conjugate base and the strongest base has the weakest conjugate acid.

10.10 Acids, Bases, and Human Health

Strong acids and bases cause damage on contact with living cells. Their action is nonspecific. All cells, regardless of type, are damaged more or less equally. These *corrosive* poisons produce what are known as chemical burns. The injuries, once the offending agent is neutralized or removed, are very similar to burns from heat. They are often treated the same way.

Sulfuric acid (H_2SO_4) is by far the leading chemical product of United States industry. Over 28 000 000 000 kg (62 000 000 000 lb) were produced in 1973. Most of this acid is used by industries. Only a small portion is used in or around the home. Automobile batteries contain sulfuric acid. It is also the major ingredient in one type of drain cleaner, presumably because it dissolves drain-clogging hair. Sulfuric acid is a powerful dehydrating agent. It takes up water from cellular fluid, rapidly killing the cell. The sulfuric acid molecules dehydrate by actually reacting with water to form hydronium ions and hydrogen sulfate ions.

$$H_2SO_4 + H_2O \longrightarrow H_3O^+ + HSO_4^-$$

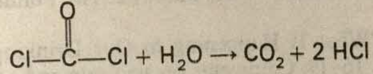
Hydration of these ions and other secondary reactions may also be involved in the dehydration process.

In section 10.7 we saw how the burning of sulfur-containing coal produces aerosol mists of sulfuric acid. When this airborne pollutant comes into contact with the alveoli of the lungs, the cells are broken down. The alveoli lose their resilience, making it difficult for them to remove carbon dioxide. Such lung damage leads to—or at least contributes to—pulmonary emphysema, a condition characterized by an increasing shortness of breath. Emphysema is the fastest growing cause of death in the United States. Most likely the principal factor in the rise of emphysema is cigarette smoking. Air pollution is known to be a factor, however. For instance, the incidence of the disease among smokers is three times as great in St. Louis, where air pollution is rather heavy, as in Winnipeg, Manitoba, where air pollution is rather mild. The U.S. Environmental Protection Agency has recently expressed concern that catalytic converters, placed on automobiles to decrease the amount of certain pollutants, might actually lead to an increase in sulfuric acid mists in urban areas. This would lead to increased human health risks. The problem continues under active study.

Hydrochloric acid (also called muriatic acid) is used in homes to clean calcium carbonate deposits from toilet bowls, and in industry to clean excess mortar from bricks and to clean and pickle metal products. Concentrated solutions (about 38% HCl) cause severe burns, but more dilute solutions are considered safe enough for use around the home. Even dilute solutions, however, can cause skin irritation and inflammation.

Ingestion of sulfuric, hydrochloric, or any other strong acid causes corrosive damage to the digestive tract. As little as 10 ml of concentrated (98%) H_2SO_4, taken internally, may be fatal.

Phosgene, used in the gas warfare of World War I, acts by reacting with moisture in the lungs to produce hydrochloric acid.



$$\mathrm{Cl{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}Cl} + \mathrm{H_2O} \rightarrow \mathrm{CO_2} + 2\,\mathrm{HCl}$$

The irritated lung tissue gives up water to the dehydrating acid, and the lungs fill with fluid. The victim dies of suffocation.

Sodium hydroxide (lye) is by far the most common of the strong bases. It is used to open clogged drains and as an oven cleaner. It destroys tissue rapidly, causing severe chemical burns. Several detergent additives, such as carbonates, silicates, and borates, form strongly basic solutions when dissolved in water. These, too, can cause corrosive damage to tissues, particularly those of the digestive tract and the eyes.

Both acids and bases, even in dilute solutions, break down the protein molecules in living cells. Generally, the fragments are not able to carry out the functions of the original protein. In cases of severe exposure, the fragmentation continues until the tissue has been completely destroyed.

Acids and bases, misused, can be damaging to human health. But acids and bases affect human health in more subtle—and ultimately more important—ways, as we shall see.

Problems

1. List four general properties of acidic solutions.
2. To what ion did Arrhenius attribute the properties of acidic solutions?
3. What is a hydronium ion? How does it differ from a hydrogen ion (proton)?
4. Give an example of a monoprotic acid, a diprotic acid, and a triprotic acid.
5. Give formulas and names of three strong acids and three weak acids.
6. If Br^- is bromide ion, what is the name of the acid HBr?
7. If NO_2^- is nitrite ion, what is the name of the acid HNO_2?
8. If $C_2O_4^{2-}$ is oxalate ion, what is the name of the acid $H_2C_2O_4$?
9. If H_4SiO_4 is orthosilicic acid, what is the formula for metasilicic acid? For metasilicate ion? For sodium metasilicate?
10. List four general properties of basic solutions.
11. To what ion did Arrhenius attribute the properties of basic solutions?
12. Give formulas and names for two strong bases and two weak bases.
13. Magnesium hydroxide is completely ionic, even in the solid state, yet it can be taken internally as an antacid. Explain why it does not cause injury as a strong base would.
14. Complete the following by writing formulas for the expected products, and then balance the equations.
    a. $Mg + HCl \rightarrow$
    b. $HCl + LiOH \rightarrow$
    c. $Na + H_2O \rightarrow$
    d. $Al(OH)_3 + HCl \rightarrow$
    e. $NaHCO_3 + HNO_3 \rightarrow$
    f. $CaCO_3 + HBr \rightarrow$
15. In each reaction below, label each reactant and product as acid or base (in the Brønsted-Lowry sense). Which acid is the strongest? Which base is the strongest? Indicate the pairs of conjugate acid and base.
    a. $CN^- + HCl \rightarrow HCN + Cl^-$
    b. $NH_3 + H_2O \rightarrow NH_4^+ + OH^-$
16. How do corrosive acids and alkalis destroy cells? (Give two ways.)

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chapter 11

More Acids and Bases

If our bodies are largely solutions—and they surely are—they are very special solutions. Delicate balances must be maintained among the many solutes in our blood and other body fluids. And no balance is more important than that between acids and bases. If the acidity of the blood changes very much, the blood loses its capacity to carry oxygen. Since many bodily processes produce acids, the control of acidity is—quite literally—a matter of life or death.

Our bodies have developed a marvelously complex yet efficient mechanism for maintaining the proper acid-base balance. Before we can talk about this mechanism in a meaningful way, however, we need to develop a few concepts—concepts which are more quantitative in nature than those developed in chapter 10. It is important to know how exact concentrations of acids and bases are determined and expressed. We must understand the concept of pH, particularly as it relates to the chemistry of the blood and other body fluids. Most important, we must see just how, through substances called buffers, the level of acidity is controlled.

11.1 Concentrations of Acids and Bases

While 1 mole of HCl just neutralizes 1 mole of NaOH, 1 mole of H_2SO_4 will neutralize 2 moles of NaOH.

$$\underset{\textit{1 mole}}{\mathrm{HCl(aq)}} + \underset{\textit{1 mole}}{\mathrm{NaOH(aq)}} \longrightarrow \mathrm{NaCl(aq)} + \mathrm{H_2O}$$

$$\underset{\textit{1 mole}}{\mathrm{H_2SO_4(aq)}} + \underset{\textit{2 moles}}{\mathrm{2\ NaOH(aq)}} \longrightarrow \mathrm{Na_2SO_4(aq)} + \mathrm{2\ H_2O}$$

In neutralization reactions, then, 1 mole of H_2SO_4 is equivalent to 2 moles of HCl, that is, will do the work of 2 moles of HCl. Alternatively, we may say that 0.5 mole of H_2SO_4 is equivalent to 1 mole of HCl. For acids and bases, some chemists find it more convenient to use *equivalent weights* rather than formula weights.

$$\text{Equivalent weight of an acid} = \frac{\text{formula weight of the acid}}{\text{number of replaceable hydrogens per molecule}}$$

$$\text{Equivalent weight of a base} = \frac{\text{formula weight of the base}}{\text{number of available hydroxides per formula unit}}$$

These definitions are perhaps best understood through examples.

Example 11.1 What is the equivalent weight of H_2SO_4?

The formula weight of H_2SO_4 is 98. There are two replaceable hydrogens; thus, the equivalent weight of H_2SO_4 is

$$\frac{98}{2} = 49$$

Example 11.2 What is the equivalent weight of aluminum hydroxide [$Al(OH)_3$]?

The formula weight of $Al(OH)_3$ is 78. There are three available hydroxides per formula; therefore, the equivalent weight of $Al(OH)_3$ is

$$\frac{78}{3} = 26$$

For monoprotic acids and for bases with one hydroxide per formula unit, the equivalent weight and the formula weight are the same.

To express concentrations of acids and bases, chemists often use the term *normality* (*N*) rather than *molarity* (*M*). A 1 *N* solution of an acid or a base is one which contains 1 equivalent weight (expressed in grams) of acid or base in 1 ℓ of solution.

$$\text{Normality} = \frac{\text{equivalents of solute}}{\text{litres of solution}}$$

Example 11.3 What is the normality of an H_2SO_4 solution which contains 3 equivalents of H_2SO_4 in 5 ℓ of solution?

$$\frac{3\text{ equivalents}}{5\,\ell} = 0.6\,N$$

Example 11.4 What is the normality of a calcium hydroxide [$Ca(OH)_2$] solution which contains 7.4 g of $Ca(OH)_2$ in 2 ℓ of solution?

The formula weight of $Ca(OH)_2$ is 74. The equivalent weight is $74 \div 2 = 37$. Thus, the number of equivalents of $Ca(OH)_2$ is

$$\frac{7.4\text{ g}}{37\text{ g/equivalent}} = 0.2\text{ equivalents}$$

Table 11.1
Concentrations of stock acids and bases

Name	Formula	Normality		Molarity	
		Dilute	*Concentrated*	*Dilute*	*Concentrated*
Hydrochloric acid	HCl	6	12	6	12
Nitric acid	HNO_3	6	16	6	16
Sulfuric acid	H_2SO_4	6	36	3	18
Phosphoric acid	H_3PO_4	—	45	—	15
Acetic acid	CH_3COOH	6	17	6	17
Ammonium hydroxide*	NH_4OH*	6	15	6	15
Sodium hydroxide	$NaOH$	6	—	6	—

*A better name, perhaps, is aqueous ammonia (NH_3); however, stock solutions are still labeled "ammonium hydroxide (NH_4OH)."

The concentration of the solution is

$$\frac{0.2 \text{ equivalents}}{2\,\ell} = 0.1\ N$$

In chapter 9, the terms *dilute* and *concentrated* were introduced to indicate relative amounts of solute for a given amount of solvent. For solutions of acids and bases, these same terms are often used in a more precise manner. For example, in a laboratory, a stock solution of "concentrated" hydrochloric acid is one which is 12 *N*. A stock bottle of hydrochloric acid labeled "dilute" contains a 6 *N* HCl solution. A concentrated sulfuric acid solution is 36 *N* H_2SO_4; dilute sulfuric acid is 6 *N*. **Table 11.1** gives a summary of concentrations of common stock acids and bases. Notice that in the table all stock solutions labeled "dilute" are 6 *N*. In contrast, the normality of "concentrated" solutions is different for different solutes. In general, the concentrated solutions are the strongest solutions commercially available.

Table 11.1 also indicates that the normality of an acid equals the molarity times the number of replaceable hydrogens. If one knows either the normality or molarity of an acid, it is a simple matter to calculate the unknown concentration.

Example 11.5 What is the normality of a 0.15 *M* H_2SO_4 solution?

The normality is $0.15 \times 2 = 0.30\ N$.

Sometimes it is necessary for a laboratory worker to make a more dilute solution from a more concentrated one. To do so, one can use the following relationship.

$$\begin{array}{c}\text{Volume}\\ \text{of the}\\ \text{concentrated}\\ \text{solution}\end{array} \times \begin{array}{c}\text{concentration}\\ \text{of the}\\ \text{concentrated}\\ \text{solution}\end{array} = \begin{array}{c}\text{volume}\\ \text{of the}\\ \text{dilute}\\ \text{solution}\end{array} \times \begin{array}{c}\text{concentration}\\ \text{of the}\\ \text{dilute}\\ \text{solution}\end{array}$$

Once again, it is easier to show the use of this equation through examples.

Example 11.6 How much concentrated H_2SO_4 (36 *N*) would you use to make 500 ml of dilute H_2SO_4 (6 *N*)?

$$V_{conc} \times 36\ N = 500\ ml \times 6\ N$$

$$V_{conc} = \frac{500\ ml \times 6\ N}{36\ N} = 83\ ml$$

Example 11.7 How much 6 N HCl would you use to make 1 ℓ of 0.5 N HCl?

$$V_{conc} \times 6\ N = 1\ \ell \times 0.5\ N$$

$$V_{conc} = \frac{1\ \ell \times 0.5\ N}{6\ N} = 0.083\ \ell \text{ or } 83\ ml$$

The relationship works just as well for solutions whose concentrations are given in molarity (or percent, for that matter).

Example 11.8 How much 18 M H_2SO_4 would you need to make 100 ml of 3 M H_2SO_4?

$$V_{conc} \times 18\ M = 100\ ml \times 3\ M$$

$$V_{conc} = \frac{100\ ml \times 3\ M}{18\ M} = 17\ ml$$

11.2 Acid-Base Titrations

Sometimes it is necessary to determine just how much acid (or base) there is in a solution of unknown concentration. This is often done by a process called *titration*. If the unknown is acidic, a certain volume of the acid is carefully measured from a buret into a flask (**figure 11.1**). The buret is a piece of laboratory glassware designed to deliver known amounts of liquid into another container. An indicator dye (section 11.3) is added to the measured volume of acid. Then a basic solution of known concentration (a "standard" base) is added from another buret, slowly and carefully, until finally just one additional drop of base changes the color of the indicator dye. This is the *end point* of the titration.

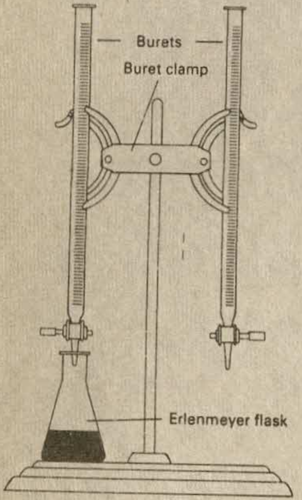


Figure 11.1 An apparatus for titration. A sample of acid of unknown concentration is measured from a buret. Base is added from another buret until an indicator changes color.

For the determination of the amount of hydroxide ion in a base of unknown concentration, the procedure is reversed. A quantity of the basic solution is measured from one buret into a flask. Then standard acid is added from the second buret until the indicator changes color. If everything is done properly, the color change (end point) occurs when the number of equivalents of base are just equal to the number of equivalents of acid (the *equivalence point*).

$$\text{Number of equivalents of acid} = \text{number of equivalents of base}$$

Recall that normality (N) is equal to the number of equivalents per litre. Rearranging the equation on page 224, we get

$$\text{Number of equivalents} = \text{normality } (N) \times \text{volume (in litres)}$$

By substituting this definition of number of equivalents into the preceding equation, we obtain a new expression for the equivalence point.

$$\text{Normality of acid} \times \text{volume of acid} = \text{normality of base} \times \text{volume of base}$$

(Notice the similarity between this equation and that used in section 11.1 for dilutions of concentrated solutions.) This equation is most useful for calculations involving titrations. We developed the equation for volumes expressed in litres, but we may use other units as long as they are the same for both acid and base. Burets are usually calibrated in millilitres, and most calculations involve this unit.

Example 11.9 Calculate the normality of 20 ml of HCl which is just neutralized by 25 ml of 0.10 *N* NaOH solution.

$$N_{HCl} \times 20\text{ ml} = 0.10\,N \times 25\text{ ml}$$

$$N_{HCl} = \frac{0.10\,N \times 25\text{ ml}}{20\text{ ml}} = 0.125\,N$$

Example 11.10 What is the concentration of an H_2SO_4 solution if 30 ml of it requires 20 ml of 0.15 *N* NaOH for neutralization?

$$N_{H_2SO_4} \times 30\text{ ml} = 0.15\,N \times 20\text{ ml}$$

$$N_{H_2SO_4} = \frac{0.15\,N \times 20\text{ ml}}{30\text{ ml}} = 0.10\,N$$

While the volume units may vary in problems such as these, it is important that concentrations be expressed as normality. Now, it is true that it will sometimes make no difference whether one uses normality or molarity. In example 11.9, one would obtain the same (and correct) answer if molarity were used. But that's because molarity equals normality for both hydrochloric acid and sodium hydroxide. The molarity of sulfuric acid solutions, however, is half their normality. This difference would introduce an error if molarity were used in example 11.10. In a titration, *equivalent* amounts of acid and base are present at the *equivalence* point. It takes only 0.5 *mole* of an acid (such as H_2SO_4) to supply a number of protons equivalent to the number of hydroxide ions released by 1 *mole* of a base (such as NaOH). By using normality, you are assured that this factor has been taken into account.

Titration is a powerful technique for the determination of the concentration of many kinds of chemicals, not just acids and bases. All that is required is a detectable change at the equivalence point. Titration can help you determine the concentration of oxidizing agents and reducing agents, the amount of silver in an ore sample, or even the activity of an enzyme.

11.3 All Power to the Protons: The pH Scale

When we think of water, we think of H_2O molecules. But even the purest water isn't all H_2O. About 1 molecule in 500 million transfers a proton to another, giving a hydronium ion and a hydroxide ion.

$$H_2O + H_2O \rightleftharpoons H_3O^+ + OH^-$$

In other words, water is in equilibrium with hydronium ion and hydroxide ion, although the equilibrium lies far to the left. The concentration of hydronium ion in pure water is 0.000 000 1, or 1×10^{-7}, mole/ℓ (M). The concentration of hydroxide ion is also 1×10^{-7} M. Pure water, then, is a neutral solution, having an *excess* of neither hydronium ions nor hydroxide ions.

The product of the hydronium ion concentration and the hydroxide ion concentration is

$$(1 \times 10^{-7})(1 \times 10^{-7}) = 1 \times 10^{-14}$$

This product, called the *ion product* of water, is sometimes represented by the symbol K_w. K_w is a constant. If you add acid to pure water, thereby increasing the concentration of hydronium ion, the concentration of hydroxide ion will fall until the product of the concentrations of the two ions equals 1×10^{-14}. Adding base to pure water will result in a similar adjustment in ion concentrations. These facts can be summarized in a single equation.

$$K_w = [H_3O^+][OH^-] = 1 \times 10^{-14}$$

The bracketed symbols are a shorthand for the concentration of the enclosed ions in moles per litre. Thus $[H_3O^+]$ should be read as the molarity of hydronium ion. The equation is valid for all aqueous solutions. And since it relates the hydronium and hydroxide ion concentrations, if the concentration of one ion is known, the concentration of the other can be calculated.

Example 11.11 Lemon juice has a $[H_3O^+]$ of 0.01 M. What is the $[OH^-]$?

In exponential form, 0.01 M is written 1×10^{-2} M. Since $[H_3O^+][OH^-] = 1 \times 10^{-14}$,

$$[OH^-] = \frac{1 \times 10^{-14}}{1 \times 10^{-2}}$$

To divide exponential numbers, one has only to subtract the exponent in the denominator from that in the numerator, so $-14 - (-2) = -14 + 2 = -12$.

$$[OH^-] = 1 \times 10^{-12}$$

Example 11.12 A sample of bile has a $[OH^-]$ of 1×10^{-6} M. What is the $[H_3O^+]$?

$$[H_3O^+] = \frac{1 \times 10^{-14}}{1 \times 10^{-6}} = 1 \times 10^{-8}$$

It is inconvenient to use exponential numbers to express the often minute concentrations of hydronium and hydroxide ion. In 1909, S. P. L. Sørensen, working in the Carlsberg Laboratory in Denmark, proposed the convenient pH scale, where

$$\mathrm{pH} = \log \frac{1}{[\mathrm{H_3O^+}]} = -\log\,[\mathrm{H_3O^+}]$$

The reaction of most people on first encountering this definition of pH is "This is more convenient?" Well, it really is. To determine the pH of a solution, you need only take the exponent of the hydronium ion concentration and reverse its sign. The pH of a solution whose hydronium ion concentration is 1×10^{-4} is 4. The point is this: it is easier to say "The pH is 4," than to say, "The hydronium ion concentration is 1×10^{-4}." They mean exactly the same thing. The pH scale has been universally adopted (even by advertising agencies for shampoo manufacturers). The relationship between pH and $[H_3O^+]$ is given in **table 11.2.** Note from the table that

$$\mathrm{pH} + \mathrm{pOH} = 14$$

A pH of 7 represents a neutral solution. A pH of less than 7 represents an acidic solution, and one of more than 7 represents a basic solution. The lower the pH, the more acidic the solution; the higher the pH the more basic the solution **(table 11.3).**

Neutral

↓

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

← *Acidic* → ← *Basic* →

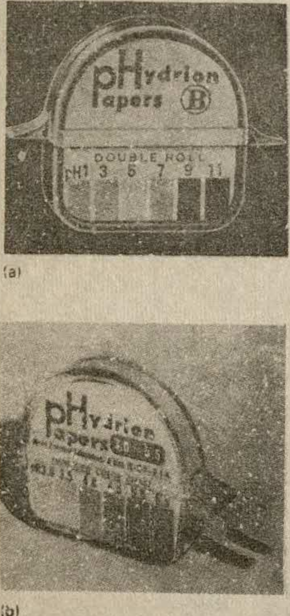
The cells in our bodies are bathed in solutions of fairly constant pH Indeed, even small changes in pH may be fatal. Many chemical reactions,

Table 11.2
The relationship between pH and $[H_3O^+]$ and between pOH and $[OH^-]$ (at 20 °C)

$[H_3O^+]$	pH	$[OH^-]$	pOH
1×10^{0}	0	1×10^{-14}	14
1×10^{-1}	1	1×10^{-13}	13
1×10^{-2}	2	1×10^{-12}	12
1×10^{-3}	3	1×10^{-11}	11
1×10^{-4}	4	1×10^{-10}	10
1×10^{-5}	5	1×10^{-9}	9
1×10^{-6}	6	1×10^{-8}	8
1×10^{-7}	7	1×10^{-7}	7
1×10^{-8}	8	1×10^{-6}	6
1×10^{-9}	9	1×10^{-5}	5
1×10^{-10}	10	1×10^{-4}	4
1×10^{-11}	11	1×10^{-3}	3
1×10^{-12}	12	1×10^{-2}	2
1×10^{-13}	13	1×10^{-1}	1
1×10^{-14}	14	1×10^{0}	0

Table 11.3
The approximate pH of some solutions

Solution	*pH*
0.1 *M* HCl	1.0
Gastric juices	1.6–1.8
Lemon juice	2.3
Vinegar	2.4–3.4
Soft drinks	2.0–4.0
Milk	6.3–6.6
Urine	5.5–7.0
Rain water (unpolluted)	6.2
Saliva	6.2–7.4
Pure water	7.0
Blood	7.35–7.45
Egg white (fresh)	7.6–8.0
Bile	7.8–8.6
Milk of Magnesia	10.5
Washing soda	12
0.1 *M* NaOH	13



(a)

(b)

Figure 11.2 Two common pH papers. (a) Wide range. (b) Narrow range. (Courtesy of Micro Essential Laboratory, Inc., Brooklyn, N.Y.)

especially those in living cells, are quite sensitive to pH. The control of pH, by compounds called buffers, is described in sections 11.5 and 11.6.

A variety of dyes, some synthetic and some from plant and animal sources, have the property of changing color over a range of pH values. We noted earlier that litmus, a vegetable dye, turns red in acidic solutions and blue in basic solutions. Actually the change occurs over a range of pH from 4.5 to 8.3. Certain combinations of indicator dyes will exhibit a whole range of colors as the pH changes from strongly basic to strongly acidic (**figure 11.2**). By selecting the proper indicator, we can determine the pH of almost any clear, colorless aqueous solution.

More accurate measurement of pH can be made electrically with pH meters. Generally, these instruments can measure pH to a precision of about 0.01 pH unit. Also, colors and turbidity generally do not interfere with electrical measurement of pH as they do with indicator color changes. Thus, pH meters can be used on blood, urine, and other complex mixtures without prior treatment of the specimen. A typical pH meter is illustrated in **figure 11.3.**

11.4 Salts in Water: Acidic, Basic, or Neutral?

When an acid reacts with a base, the products are a salt and water. The process is called neutralization, but is the solution neutral? What if we simply take a salt and dissolve it in water? Would the solution be acidic, basic, or neutral? Although we might well expect a salt solution to be neutral, not all of them are. There are many neutral salts, including the familiar sodium chloride and others such as potassium sulfate and sodium nitrate. Some, such as ammonium nitrate and aluminum chloride, are acidic. Others, such as sodium acetate and potassium cyanide, are basic.

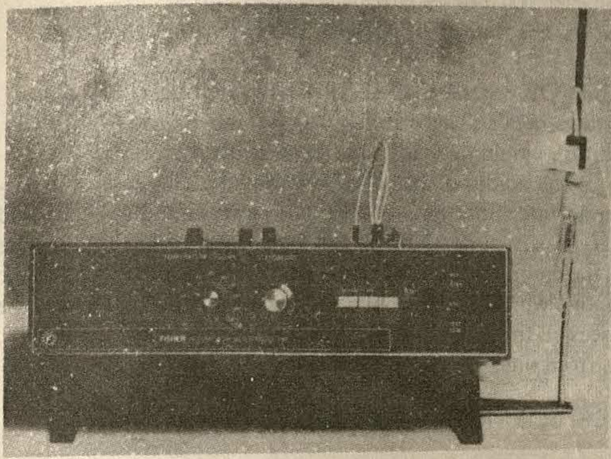


Figure 11.3 A pH meter. (Courtesy of Fisher Scientific Company, Pittsburgh.)

How do we tell if a salt is acidic, basic, or neutral? Simple. Just dissolve some of the salt in water and test the solution with indicator paper or with a pH meter. That is the experimental way, and who can argue with it? There is another way, though. We can *predict* whether a solution of a salt will be acidic, basic, or neutral by considering the relative strengths of the acid and base from which the salt was made. Just think how much more convenient it is to apply a rule than to go into a laboratory and do an experiment. The rules are as follows.

1. The salt of a strong acid and a strong base forms a neutral solution.
2. The salt of a strong acid and a weak base forms an acidic solution.
3. The salt of a weak acid and a strong base forms a basic solution.
4. The salt of a weak acid and a weak base may form an acidic, a basic, or (by chance) a neutral solution.

To apply these rules you must be able to recognize strong acids, strong bases, weak acids, and weak bases. After reviewing sections 10.2 and 10.4, look at the formula of the salt. Pair the positive ion with a number of hydroxide ions equivalent to the positive charge to get the base from which the salt could be formed. Then put one or more protons (H^+) with the negative ion of the salt to get the acid.

Example 11.13 From what acid and what base is the salt NaCl formed? Does NaCl form an acidic, basic, or neutral solution?

The positive ion in NaCl is Na^+. Na^+ requires one OH^-; the base is NaOH. The negative ion in NaCl is Cl^-. Cl^- requires one H^+; the acid is HCl. Since NaOH is a strong base and HCl is a strong acid, then, according to rule 1, NaCl is a neutral salt.

Example 11.14 Is a solution of $(NH_4)_2SO_4$ acidic, basic, or neutral?

The base is NH_4OH (really aqueous NH_3) and the acid is H_2SO_4. Since aqueous NH_3 is a weak base and H_2SO_4 is a strong acid, the solution is acidic (rule 2).

Example 11.15 Is a solution of CH_3COOK acidic, basic, or neutral?

The base, KOH, is a strong one. Acetic acid, CH_3COOH, is a weak acid. The solution is basic (rule 3).

Example 11.16 Is a solution of CH_3COONH_4 acidic, basic, or neutral?

The base, NH_4OH (aqueous NH_3), is a weak one. The acid, CH_3COOH, is also weak. There is no way to tell from the rules whether the solution would be acidic, basic, or neutral (rule 4).

Why should a salt be acidic or basic? Let's consider the case of a particular salt, sodium acetate. Solutions of this salt contain sodium ions and acetate ions, each type surrounded by water molecules. Now the acetate (CH_3COO^-) ion is the conjugate base of acetic acid (section 10.9). And acetic acid is a weak acid, one which does not like to give up a proton. The acetate ion looks around, sees all those lovely water molecules with their hydrogens, and grabs a proton from one.

$$CH_3COO^- + H_2O \rightarrow CH_3COOH + OH^-$$

This makes the acetic acid molecule fairly content because it has gained back the proton it hates to lose. Unfortunately, the water molecule which has just given up the proton is not at all happy. Water is also a weak acid, even weaker than acetic acid, and it will fight effectively to keep the proton and usually will win.

$$CH_3COO^- + H_2O \rightleftharpoons CH_3COOH + OH^-$$

All this means that there is an equilibrium established in which the two acids, water and acetic acid, struggle to keep the proton, and the equilibrium is shifted stongly to the left. Nonetheless, there is an equilibrium, and some undissociated acetic acid and some excess hydroxide ions are present in the solution. Those hydroxide ions are what makes the solution basic.

It is important to note that there is no analogous equilibrium which results in extra hydronium ions to balance the hydroxide ions. The sodium ions, the other half of the salt in our example, have no tendency to react with water to produce extra hydronium ions. We could write an equation to suggest the possibility.

$$Na^+ + 2\,H_2O \rightarrow NaOH + H_3O^+$$

But sodium hydroxide is a strong base and is completely ionized, so to be correct we would have to write

$$Na^+ + 2\,H_2O \rightarrow Na^+ + OH^- + H_3O^+$$

Since sodium ion appears on both sides of the equation, this reaction would boil down to

$$2\,H_2O \rightarrow H_3O^+ + OH^-$$

which is simply a restatement of the fact that water itself ionizes slightly. The slight ionization of water gives equal amounts of hydronium ion and hydroxide ion, whereas the equilibrium involving the acetate ion (above) gives a small amount of excess hydroxide ion. The salt of a strong base and a weak acid gives a slightly basic solution.

For a solution of the salt of a weak base and a strong acid, precisely the opposite happens. Thus, for ammonium chloride (NH_4Cl), the ammonium ion exists in equilibrium with its conjugate base.

$$NH_4^+ + H_2O \rightleftharpoons H_3O^+ + NH_3$$

Ammonia, although a weak base, is a stronger base than water, so the equilibrium is shifted to the left. However, some excess hydronium ion is present in the solution because of this equilibrium. The chloride ion from ammonium chloride has no tendency to pick up a proton from water to form undissociated hydrochloric acid and hydroxide ion, because hydrochloric acid is a strong acid and chloride ion simply won't accept the proton. The solution of a salt of a strong acid and a weak base contains excess hydronium ion and is slightly acidic.

In a solution of sodium chloride, neither ion has a tendency to enter equilibrium with water molecules, and neither excess hydroxide ion nor hydronium ion is present. The solution is neutral.

Finally, both ions from a salt of a weak acid and a weak base enter equilibria. The solution of such a salt can be acidic, basic, or neutral; depending on which equilibrium predominates, that is, how much to the left or right each equilibrium is shifted.

11.5 Buffer Zone: Control of pH

Who cares about the pH of a salt solution anyway? You do, that's who, for some of these salts play a vital role in the control of the pH of body fluids. If they should fail to function, so will you. Our bodies are acid factories. Our stomachs produce hydrochloric acid. Our muscles produce lactic acid. Starches and sugars produce pyruvic acid when metabolized. Carbon dioxide from respiration produces carbonic acid in the blood. Our bodies must eliminate or neutralize these acids, because excess acidity in the wrong place would kill us rather quickly.

A *buffer solution* is one in which the pH remains relatively constant even if acid or base is added. Chemically, a buffer solution is one which contains a weak acid and one of its salts (or a weak base and one of its salts), usually in approximately equal concentrations. For example, 1 ℓ of a solution which contains 0.1 mole of acetic acid (CH_3COOH) and 0.1 mole of sodium acetate (CH_3COONa) acts as a buffer at pH 4.74, a somewhat acidic value.* This buffer can absorb significant amounts of additional acid or base with-

*This may be a bit confusing since we have just spent some time considering the fact that a solution of sodium acetate is slightly basic (i.e., has a pH greater than 7). However, it is a solution containing *only* the salt which is basic. The buffer solution consists not only of a salt of acetic acid but also of some acetic acid itself. It is the presence of this acid that makes this buffer solution acidic.

out appreciable change in pH. For instance, the addition of 10 ml of 0.1 *M* NaOH to this buffer causes a pH change of only 0.01 pH unit. If that amount of base were added to 1 ℓ of pure water, the pH would change by 4 full pH units. The buffer system is what prevents such a large change in pH.

How does a buffer work? It may seem strange that a solution can absorb acid or base without the pH changing appreciably. The explanation, however, is fairly simple (although you may feel free to dispute that). The buffer solution has a large reservoir of both acid molecules and the conjugate base of the acid (anions from the salt). If a strong acid is added, the hydronium ions from the added acid will donate protons to the anions of the buffer to form the weak acid and water.

$$H_3O^+ + CH_3COO^- \rightleftharpoons CH_3COOH + H_2O$$

Although the reaction is reversible to a slight extent, most of the protons are removed from the solution as they are added, and the pH changes hardly at all.

When a strong base is added, the hydroxide ions will react with the hydronium ions formed in the solution by the acetic acid of the buffer.

$$OH^- + H_3O^+ \longrightarrow 2\ H_2O$$

The added hydroxide ions are tied up, and the hydronium ions removed from the solution are immediately replaced by further ionization of the acetic acid in the buffer.

$$CH_3COOH + H_2O \rightleftharpoons CH_3COO^- + H_3O^+$$

The concentration of hydronium ions returns to approximately the original value, and the pH is only slightly changed.

There are many important buffer solutions. Most biochemical reactions, whether they occur in a laboratory or in our bodies, are carried out in buffered solutions. The buffers that control the pH of our blood will be discussed in the next section. **Table 11.4** lists some buffers of interest and the pH range in which they operate.

Table 11.4
Some important buffers and the pH of a solution which is 0.1 *M* in each compound (at 25 °C)

Buffer	*pH*
$CH_3CHOHCOOH/CH_3CHOHCOO^-$	3.86
CH_3COOH/CH_3COO^-	4.76
$H_2PO_4^-/HPO_4^{2-}$	7.20
H_2CO_3/HCO_3^-	6.46*
NH_4^+/NH_3	9.25

*This value includes dissolved CO_2 molecules as undissociated H_2CO_3. The value for just H_2CO_3 is about 3.8.

11.6 Buffers in Blood

The pH of the blood of higher animals is held remarkably constant. In humans, blood plasma normally varies from 7.35 to 7.45 in pH. Should the pH rise above 7.8 or fall below 6.8, due to starvation or disease, the patient may suffer irreversible damage to the brain or even die. Fortunately, human blood has not one, but at least three, buffering systems. Of these, the bicarbonate/carbonic acid (HCO_3^-/H_2CO_3) buffering system is the most important.

If acids are put into the blood, hydronium ions are taken up by the bicarbonate ions to form undissociated carbonic acid and water.

$$HCO_3^- + H_3O^+ \longrightarrow H_2CO_3 + H_2O$$

As long as there is sufficient bicarbonate to take up the added acid, the pH will change little.

The carbonic acid is a weak acid and exists in equilibrium with hydronium and bicarbonate ions.

$$H_2CO_3 + H_2O \rightleftharpoons H_3O^+ + HCO_3^-$$

If bases come into the bloodstream, reacting with hydronium ions to form water, more carbonic acid molecules will ionize to replace the removed hydronium ions. Further, as the carbonic acid molecules are used up, more carbonic acid can be formed from the large reservoir of dissolved carbon dioxide in the blood.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3$$

Thus, bicarbonate/carbonic acid buffers the blood against either added base or added acid.

Another blood buffer is the dihydrogen phosphate/monohydrogen phosphate ($H_2PO_4^-/HPO_4^{2-}$) system. Any acid reacts with monohydrogen phosphate to form dihydrogen phosphate.

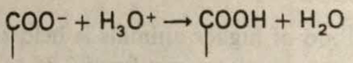
$$HPO_4^{2-} + H_3O^+ \longrightarrow H_2PO_4^- + H_2O$$

The dihydrogen phosphate is a weak acid and exists in equilibrium with hydronium ions and monohydrogen phosphate.

$$H_2PO_4^- + H_2O \rightleftharpoons H_3O^+ + HPO_4^{2-}$$

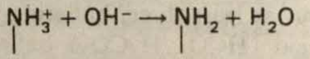
Any base that comes into the blood would react with hydronium ions to form water. However, more dihydrogen phosphate would ionize to replace these hydronium ions, leaving the pH essentially unchanged.

Proteins act as a third type of blood buffer. These complex molecules (chapter 24) contain $-COO^-$ groups, which, like acetate ions (CH_3COO^-), can act as proton acceptors. Proteins also contain $-NH_3^+$ groups, which, like ammonium ions (NH_4^+), can donate protons. If acid comes into the blood, hydronium ions can be neutralized by the $-COO^-$ groups.



$$-COO^- + H_3O^+ \rightarrow -COOH + H_2O$$

If base is added, it can be neutralized by the $—NH_3^+$ groups.

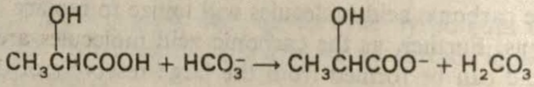


$$-NH_3^+ + OH^- \rightarrow -NH_2 + H_2O$$

These three buffers (and perhaps others) act to keep the pH of the blood constant. Buffers can be overridden by large amounts of acid or base; their capacity is not infinite. The blood buffers can be overwhelmed if the body's metabolism goes badly awry.

11.7 Personal pH Problems: Acidosis and Alkalosis

Have you ever had your muscles hurt after prolonged physical acitivity? If so, you have had your blood buffers somewhat overloaded. Muscle contraction produces lactic acid. This acid ionizes somewhat more strongly than carbonic acid and thus tends to lower the pH of the blood (it tends to release more hydronium ions into the blood). Moderate amounts of lactic acid can be handled by the blood buffers. For bicarbonate, the reactions would be



$$CH_3CH(OH)COOH + HCO_3^- \rightarrow CH_3CH(OH)COO^- + H_2CO_3$$

Lactic acid *Lactate ion*

Excessive amounts of lactic acid overload the buffers, however, and the pH is lowered. Nerve cells respond to the increased acidity by sending a message of pain to the brain.

If the pH of the blood falls below 7.35, the condition is called *acidosis*. If the pH of the blood rises above 7.45, *alkalosis* sets in. These pathological conditions can be caused by faulty respiration or by metabolic problems. In severe cases of starvation, the body gets its energy by the oxidation of stored fats. The products of fat metabolism are acidic, and prolonged starvation leads to acidosis. Fad diets, such as those that severely limit the intake of carbohydrates, can also lead to acidosis.

The body's excretory system tries to compensate for acidosis or alkalosis by selectively excreting certain compounds. Conversely, the conditions can be brought on by kidney failure or other excretory problems. We will discuss these pathological problems further in later chapters.

Problems

1. Calculate the formula weight and equivalent weight of each of the following compounds.
   a. HBr c. H_2S e. H_3PO_3 g. CH_3COOH
   b. LiOH d. $Ba(OH)_2$ f. H_2SiO_3
2. Calculate the normality of each of these solutions.
   a. 3 equivalents of H_3AsO_4 in 6 ℓ of solution
   b. 20 g of NaOH in 0.5 ℓ of solution
   c. 9.8 g of H_2SO_4 in 0.2 ℓ of solution

d. 342 g of $Ba(OH)_2$ in 10 ℓ of solution
e. 12 g of CH_3COOH in 100 ml of solution

3. What is the normality of a 3.0 *M* solution of $Ba(OH)_2$?
4. What volume of concentrated (36 *N*) sulfuric acid would be required for the following to be made?
   a. 12 ℓ of 6 *N* solution?
   b. 500 ml of 0.10 *N* solution?
5. Calculate the normality of an HCl solution if 20 ml of it requires the following for neutralization.
   a. 40 ml of 0.25 *N* NaOH
   b. 10 ml of 0.50 *N* KOH
6. A 20-ml sample of gastric fluid is neutralized by 25 ml of 0.10 *N* NaOH. What is the normality of HCl in the fluid? Assume that all the acidity of the gastric fluid is due to HCl.
7. What is the pH of each of these solutions?
   a. 0.01 *M* in HCl
   b. 0.0001 *M* in HCl
   c. 0.1 *M* in NaOH
   d. 0.001 *M* in NaOH
   e. 0.00001 *M* in HNO_3
   f. 0.01 *M* in KOH
   g. 0.001 *M* in HNO_3
8. Indicate whether each of the following pH values represents an acidic, a basic, or a neutral solution.
   a. 11
   b. 4
   c. 7
   d. 3.4
9. Write an equation for the equilibrium established when each of these ions is placed in water.
   a. CH_3COO^-
   b. CN^-
   c. NH_4^+
10. Classify the aqueous solution of each of these salts as acidic, basic, or neutral.
    a. KCl
    b. NaCN
    c. NH_4CN
    d. CH_3COOK
    e. $(NH_4)_2SO_4$
    f. Na_2SO_4
11. A weak acid is titrated with a strong base. Would the solution at the end point be acidic, basic, or neutral? Explain.
12. Use acetic acid and acetate ion to explain how a buffer controls pH.

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chapter 12

Electrolytes

The term *ion* was introduced in chapter 2 to describe charged particles produced in cathode-ray tubes. We have come a long way since then, and along the way we've discussed ionic bonds, ionic solids, and solutions of ions. The 19th-century scientists whose experiments laid the foundation for the ionic theory were working mainly for the joy of discovery and the recognition gained with success. We can only speculate whether they imagined the importance of ions in living systems.

It is now well established that messages are sent to and from the brain in the form of electrical signals. These messages are often carried by ions through cellular and intercellular fluids. Certain ions are essential to the proper functioning of all living organisms. They must be present in proper concentrations, however. Too little or too much can be dangerous. We will discuss some of these ions and their properties in this chapter.

12.1 The Earliest Electricians

In 1800, an Italian physicist, Alessandro Volta, invented a battery which produced an electric current. Electrical phenomena had already been subjected to considerable study before this time. (In 1752, Benjamin Franklin received an electric shock while flying a kite during a thunderstorm to determine whether lightning was a form of electricity.) The importance of Volta's invention lay in the fact that the battery provided a convenient source of electricity, one which could be used by other scientists who wished to study the interaction of matter and electricity.

Within 6 weeks of its invention, a battery was used by two English chemists, William Nicholson and Anthony Carlisle, to decompose water into hydrogen gas and oxygen gas. They accomplished the decomposition by passing an electric current through the water sample. Sir Humphrey Davy, another English chemist, used an electric current to liberate potassium metal from potassium hydroxide (KOH), sodium metal from sodium hydroxide

(NaOH), and metallic magnesium, strontium, barium, and calcium from their respective compounds.

Sir Humphrey's protégé, Michael Faraday, termed the process of splitting compounds by means of electricity *electrolysis*, a word of Greek origin which literally means "loosing by electricity." It was Faraday who was responsible for many of the terms used in electrochemistry today. Some of these terms were introduced in chapter 2, but we will offer a brief review here. The carbon rods or metal strips which are connected to a source of electricity (the battery) and inserted into solutions under study are called *electrodes* (examine Volta's original battery in **figure 12.1**). Electricity, we know now, is a flow of electrons. In systems used by electrochemists, electrons flow from one electrode to the other. The electrode which has lost electrons and is therefore *positively charged* is called the *anode*. The electrode which has gained electrons and is *negatively charged* is called the *cathode*. In Faraday's studies, electrodes were placed in certain solutions and melts (section 12.2). When this was done, the electric "circuit" was completed. The battery provided the driving force (the electrical potential or voltage), and electric current flowed from one electrode to the other, through the solution, and back to the first electrode, that is, around the circuit. Faraday hypothesized that the electric current was carried through the solution (or melt) by atoms which had electrical charges and which he called *ions*, a term we have used extensively in many of the preceding chapters. You will recall that *positively charged ions*, which are attracted to the negatively charged electrode (the cathode), are

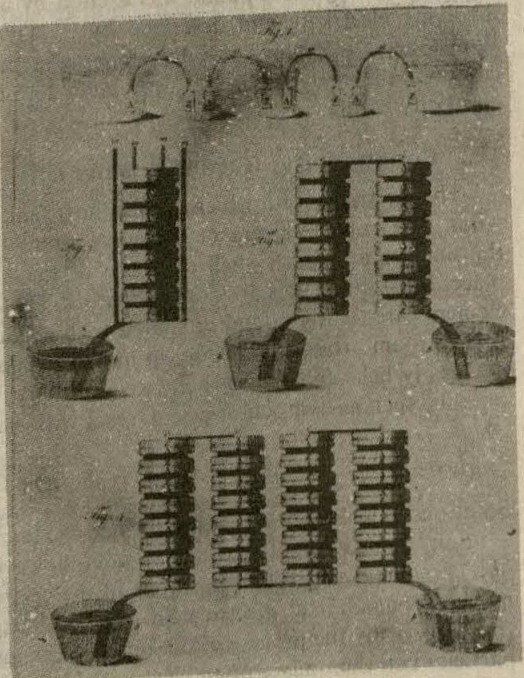


Figure 12.1 Diagrams of Volta's apparatus for the production of electric current.

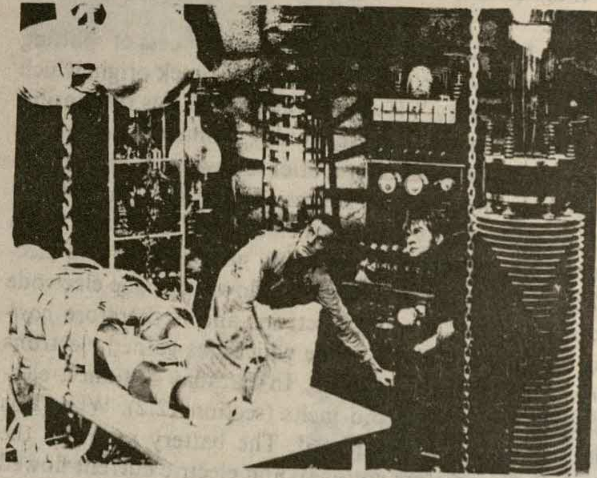


Figure 12.2 The laboratory of Frankenstein, with its apparatus for the production of electric current. (The Bettmann Archive.)

called *cations* and that *negatively charged ions*, which are attracted to the positively charged anode, are called *anions*.

The work of Faraday and other pioneers in electrochemistry generated a great deal of interest and excitement among scientists whose concern was the fundamental structure of matter. It is worth noting, however, that the interest of the general public was excited by a purely fictional experiment involving electricity and described by a 21-year-old woman. It is Mary Wollstonecraft Shelley's novel *Frankenstein*, published in 1818, which has captured the imagination of 19th- and 20th-century readers by relating electricity to life.

12.2 Conductivity: Getting a Glow On

The electricity with which we are most familiar usually flows in metallic wires. The outer electrons of the metal atoms flow through the wire, while the nucleus and inner shell electrons of the atom remain nearly fixed in place. Most nonmetals are nonconductors. The outer shell electrons of these elements are tightly bound or shared with neighboring atoms. They are not free to roam around. Likewise, in most covalent compounds, the electrons are firmly held and cannot conduct electricity. A few polar covalent compounds, such as hydrochloric acid, react with water to form ions.

$$HCl + H_2O \longrightarrow H_3O^+ + Cl^-$$

Solutions in which these ions are formed are then able to conduct electricity.

Solid ionic compounds such as salts, however, do not conduct electricity. The ions occupy fixed positions in the crystal lattice and are unable to move very much in an electric field. When the lattice is broken down by heat (melting) or by the process of dissolution, the ions are freed. These charged particles can then move in an electric field. Substances which conduct electricity as melts or in solutions are called *electrolytes*.

How do we know an electrolyte when we see one? Simple. Just dissolve some of the compound in water and test it with a conductivity apparatus (**figure 12.3**). If a solution which conducts electricity is placed in the dish, thus completing the circuit, electric current will flow in the apparatus pictured in **figure 12.3**, and the light bulb will glow. Those compounds which, in aqueous solution, are good conductors (i.e., those which cause the bulb to glow brightly) are called *strong electrolytes.* Those compounds whose aqueous solutions produce only a dim light are called *weak electrolytes.* Other compounds, whose solutions don't light the bulb at all, are called *nonelectrolytes.* These compounds produce few if any ions in solution and conduct no appreciable current.

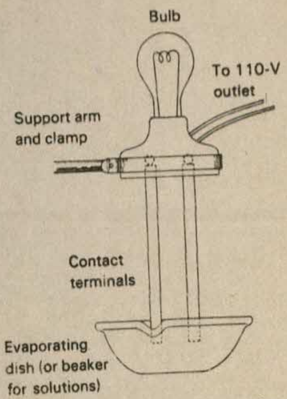


Figure 12.3 An apparatus for testing the electrical conductivity of solutions.

Isn't there an easier way to determine whether a compound is an electrolyte? Can we predict electrical conductivity? Indeed we can, at least in many cases. All strong acids and strong bases (chapter 10) and all salts that are appreciably soluble in water are strong electrolytes. All weak acids and weak bases and some slightly soluble salts are weak electrolytes. Molecular substances, such as sugar and alcohol, which are neither acids nor bases, are nonelectrolytes. The deciding factor in all cases is the ability of the compound being considered to provide ions in aqueous solution. **Table 12.1** lists some familiar compounds and the behavior of their solutions toward electrical current.

12.3 Up with Boiling Points, Down with Freezing Points

We use salt to melt ice on sidewalks and roadways. How does salt melt ice? Is it hot salt? No, the phenomenon is related to a property of solutions we mentioned in chapter 9. On contact with ice, some of the salt dissolves. The salt solution produced has a lower freezing point than the pure ice and exists as a liquid at a lower temperature than pure water, so, even on a cold day, the ice on a sidewalk will melt if it is brought into contact with salt.

We saw in chapter 9 that molecular substances such as ethylene glycol can lower the freezing point of water. A mole of ethylene glycol lowers the

Table 12.1

A selection of strong electrolytes, weak electrolytes, and nonelectrolytes

Compound Name	*Formula*	*Kind of Compound*	*Electrical Conductivity*
Hydrochloric acid	HCl	Strong acid	Strong
Sulfuric acid	H_2SO_4	Strong acid	Strong
Sodium hydroxide	$NaOH$	Strong base	Strong
Sodium chloride	$NaCl$	Salt	Strong
Calcium nitrate	$Ca(NO_3)_2$	Salt	Strong
Acetic acid	CH_3COOH	Weak acid	Weak
Ammonia	NH_3	Weak base	Weak
Calcium sulfate	$CaSO_4$	Slightly soluble salt	Weak
Copper(II) sulfide	CuS	Insoluble salt	None
Sugar (sucrose)	$C_{12}H_{22}O_{11}$	Molecular solid	None
Ethyl alcohol	C_2H_5OH	Molecular liquid	None

freezing point of 1 kg of water by 1.86 °C. Why not use ethylene glycol (or alcohol or sugar) to remove ice from sidewalks? We could, but sodium chloride does a better job of it, mole for mole. A mole of sodium chloride lowers the freezing point nearly twice as much as a mole of ethylene glycol. Why? Is it a coincidence that the salt is an electrolyte and ethylene glycol and sugar and alcohol are not? No, it's not. Freezing-point depression depends on the *number* (not kind) of particles in a given amount of solvent. Electrolytes are compounds which produce ions in solution. Sodium chloride exists as sodium ions and chloride ions in solution. There are twice as many particles in a mole of sodium chloride as there are in a mole of ethylene glycol. A mole of the latter has 6.02×10^{23} particles (molecules). A mole of sodium chloride has 12.04×10^{23} particles (6.02×10^{23} sodium ions plus 6.02×10^{23} chloride ions).

Calcium chloride ($CaCl_2$) is even better for clearing ice from sidewalks. It depresses the freezing point of water nearly three times as much as a molecular substance because each unit of calcium chloride furnishes three particles, one calcium ion and two chloride ions.

$$CaCl_2(s) \longrightarrow Ca^{2+}(aq) + 2\ Cl^-(aq)$$

Calcium chloride is sometimes used in place of sodium chloride for ice removal. Why not use calcium chloride in place of ethylene glycol in automobile radiators? It's too corrosive. It is used as an antifreeze in some commercial operations, however.

Boiling points are elevated more than the usual amount by electrolytes. A mole of sodium chloride elevates the boiling point of water nearly twice as much as does a mole of sugar. And a mole of calcium chloride raises it nearly three times as much.

Osmotic pressure (chapter 9) is still another property that depends on the number, not the kind, of particles present in solution. Electrolytes, mole for mole, give higher osmotic pressures than nonelectrolytes. As you might guess, the variation is about the same as that for freezing-point depression and boiling-point elevation. The importance of electrolytes in maintaining proper osmotic pressures within and outside of living cells cannot be overemphasized. The cell membranes are selectively permeable to small ions. Proper distribution of these ions (electrolyte balance) ensures that the body's cells neither rupture nor collapse due to an imbalance in osmotic pressures.

12.4 The Theory of Electrolytes: Ionization and Dissociation

In 1887 Svante Arrhenius proposed a general theory to explain the properties of electrolytes. We encountered a part of that theory in chapter 10 in our study of acids and bases. Further, Arrhenius' theory has been modified somewhat through the years to account for new data. The modernized theory is summarized here.

1. An electrolyte, when dissolved in water, dissociates into ions, each of which carries an electric charge. For salts, this process may be summarized by an equation. For example,

$$Na_2SO_4(s) \rightarrow 2\ Na^+(aq) + SO_4^{2-}(aq)$$

$$CaCl_2(s) \rightarrow Ca^{2+}(aq) + 2\ Cl^-(aq)$$

For acids and some bases, the process is actually one of *ion formation*, or *ionization*.

$$HCl(g) + H_2O \rightarrow H_3O^+(aq) + Cl^-(aq)$$

$$NH_3(g) + H_2O \rightarrow NH_4^+(aq) + OH^-(aq)$$

For strong bases, the process is usually one of dissociation, that is, separation of already existing ions.

$$NaOH\ (s) \rightarrow Na^+(aq) + OH^-(aq)$$

2. When an ionic solid dissociates or when a polar molecule ionizes, the algebraic sum of all positive charges and all negative charges is 0.

$$K_3PO_4(s) \rightarrow 3\ K^+(aq) + PO_4^{3-}(aq)$$

$$3(+1) + (-3) = 0$$

   Solutions as a whole are therefore electrically neutral.
3. Each ion, regardless of size, charge, or shape, has the same effect on boiling-point elevation, freezing-point depression, and osmotic pressure as an undissociated molecule would have. This assumption holds quite well for dilute solutions but is not strictly true for concentrated ones. In concentrated solutions, each ion is rather closely surrounded by others of opposite charge. This hinders the movement of the ions; they are not completely free. This decreases the expected activity somewhat. For example, the freezing-point depression of a solution of 1 mole of NaCl in 1 kg of water is 1.8 times (not quite twice) that of a nonelectrolyte at the same concentration.
4. Weak electrolytes react with water to a limited extent and hence provide only a limited number of ions in solution.
5. Nonelectrolytes exist in molecular form in solution or are insoluble salts; they produce no appreciable concentration of ions.

12.5 Electrolysis: Chemical Change Caused by Electricity

If sodium chloride is heated until it melts, the molten salt conducts electricity, as one can see by testing the melt in the conductivity apparatus in **figure 12.3.** In addition to causing the light bulb to glow, the electric current, as it passes through the melt, causes observable chemical changes. Yellow-green chlorine gas forms at the anode. At the cathode, silvery metallic sodium is formed and is rapidly vaporized by the hot melt. The molten, ionic sodium chloride is decomposed by electrical energy into elemental sodium and chlorine.

$$2\ NaCl + \text{energy} \rightarrow 2\ Na + Cl_2$$

In crystalline form, sodium chloride does not conduct electricity. The ions occupy relatively fixed positions in the lattice and do not move very much, even under the influence of an electrical potential. When sodium chloride melts, the ions are freed to move around. When a battery is connected to the melt through a pair of electrodes, the sodium ions are attracted to the electron-rich cathode, where they pick up electrons (**figure 12.4**).

$$Na^+ + e^- \longrightarrow Na$$

The chloride ions migrate to the electron-poor anode, where they give up electrons.

$$2\ Cl^- \longrightarrow Cl_2 + 2\ e^-$$

The battery in the circuit is responsible for seeing to it that this exchange of electrons does not eventually lead to neutralized electrodes. Electrons picked up by the anode from chloride ions are immediately shunted, under the influence of the battery, to the cathode, which has been losing electrons to sodium ions. As long as sodium ions and chloride ions are present in the melt, current will flow. When all of the salt has been converted to elemental sodium and chlorine the circuit will be broken and current will cease.

This electrolytic reaction is an oxidation-reduction process. Oxidation occurs at the anode, where the oxidation number of chlorine goes from −1 to 0. At the cathode, the oxidation number of sodium is reduced from +1 to 0.

Electrolysis, then, is a process of using electricity to bring about chemical change. The process is useful for the preparation and purification (refining) of many metals. Electrolysis is also used for coating one metal with another, an operation called electroplating. Usually the object to be electro-

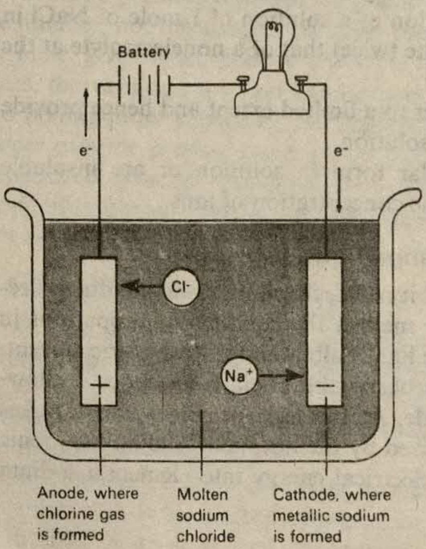

Battery
e⁻
e⁻
Cl⁻
Na⁺
+
−
Anode, where chlorine gas is formed
Molten sodium chloride
Cathode, where metallic sodium is formed

Figure 12.4 The electrolysis of molten sodium chloride.

plated, such as a spoon, is cast of a cheaper metal. It is then coated with a thin layer of a more attractive and more corrosion-resistant metal, such as gold or silver. The cost of the finished product is far less than that of a corresponding item made entirely of silver or gold. A cell for the electroplating of silver is shown in **figure 12.5.** The silver is made the anode, and the spoon is made the cathode. A solution of silver nitrate is used as the electrolyte. Under the influence of the battery in the system (or any voltage source), the silver ions (Ag^+) are attracted to the cathode (spoon), where they pick up electrons and are deposited as silver atoms.

$$Ag^+ + e^- \longrightarrow Ag$$

At the anode, electrons are removed from the silver bar. Some of the silver atoms lose electrons to become silver ions.

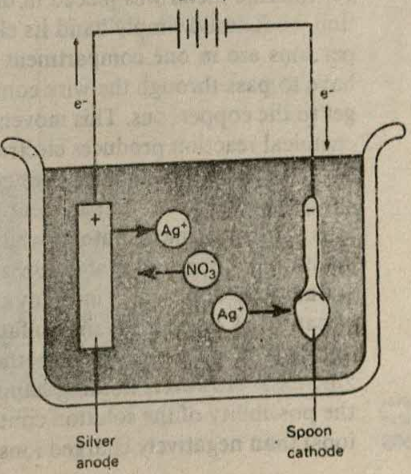
$$Ag \longrightarrow Ag^+ + e^-$$

The net process is one in which the silver from the bar is transferred to the spoon. The thickness of the deposit can be controlled by accurate measurement of the amount of current flow and of the duration of the process.

Electrolysis finds some biological applications, including the removal of unwanted hair. In this process, a tiny wire needle is used to supply a mild electrical current to the hair root. The chemical changes engendered there kill the living follicle. This is perhaps the only permanent method of hair removal. In the hands of a skilled technician, the method can be clean and safe. It is tedious, however, for each hair root must be treated individually. Similar procedures are sometimes used for the removal of warts or other growths.

Electrical processes once made up a large part of medical quackery and are still sometimes used in unethical ways. For an interesting discussion of some of these, see reference 8.

Figure 12.5 An electrolytic cell for the plating of silver.



12.6 Hearts, Brains, and Other Batteries

Electricity can cause chemical change. Conversely, chemical change can produce electricity. That's what batteries are all about.

If a strip of zinc metal is placed in a solution of zinc sulfate, zinc atoms exhibit a certain tendency to go into solution as zinc ions.

$$Zn \longrightarrow Zn^{2+} + 2\ e^-$$

The two electrons are left behind on the zinc strip. On the other hand, the zinc ions in solution have a tendency to migrate to the zinc strip, acquire two electrons, and be deposited as zinc atoms.

$$Zn^{2+} + 2\ e^- \longrightarrow Zn$$

The system rapidly comes to equilibrium.

$$Zn \rightleftharpoons Zn^{2+} + 2\ e^-$$

This equilibrium is affected by temperature, concentrations, and other factors described in chapter 5. For example, adding more zinc ions would shift the reaction to the left, using up zinc ions.

If a copper strip is added to a solution of copper sulfate, a similar equilibrium is established.

$$Cu \rightleftharpoons Cu^{2+} + 2\ e^-$$

Each metal differs in its tendency to give up electrons (remember the activity series of chapter 10). Copper is less likely to do so than is zinc. Now, if we connect the copper strip to the zinc strip, a current (electrons) will flow from the zinc to the copper (**figure 12.6**). In order to ionize, zinc metal forces the copper ions to accept its electrons. When we discussed the activity series in chapter 10, we described a similar reaction. The difference between the present reaction and that previously considered is that, in the reaction of chapter 10, the zinc metal was placed in direct contact with the copper ions in solution, so it could simply hand its electrons to the copper ions. Here, the copper ions are in one compartment and the zinc is in another. The electrons have to pass through the wire connecting the electrodes (the metal strips) to get to the copper ions. This movement of electrons is an electric current. The chemical reaction produces electricity.

This battery is slightly more complicated than indicated by the diagram in **figure 12.6.** The compartment containing zinc ions also contains sulfate ions. The salt, zinc sulfate, is what is dissolved in the solution. Similarly the solution of copper ions also contains sulfate ions (from copper sulfate). The sulfate ions don't enter into any chemical reaction, but they do cause complications. Consider the zinc sulfate solution. During the reaction, zinc atoms are converted to zinc ions, so the solution becomes more concentrated in zinc ions. However, nothing happens to the sulfate ions. We are faced with the possibility of the solution containing more positively charged ions (Zn^{2+} ions) than negatively charged ions (SO_4^{2-} ions). The solution will simply not

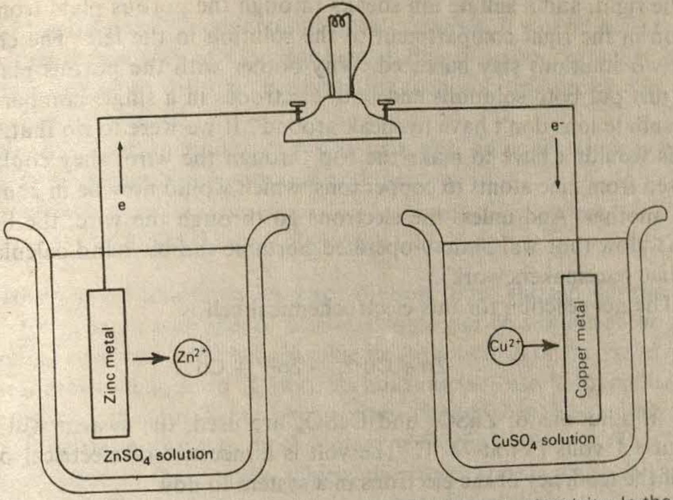
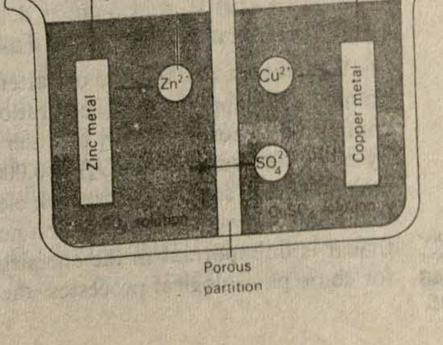


Figure 12.6 An attempt to convert chemical energy to electricity. In the left compartment, zinc atoms would give up electrons, and, in the right, copper(II) ions would pick up electrons. This electrochemical cell will not work, however.

stand for this, and if something isn't done about the imbalance, the electrolysis reaction will stop. In the other compartment of **figure 12.6**, the concentration of copper ions is being reduced while the concentration of sulfate ions remains constant. Thus, there is a tendency for this compartment to develop an excess of negatively charged ions. One way to deal with the problem is to connect the two solutions through a porous plate, made of a material which will retard the mixing of the metal ions in solution and still permit passage of sulfate ions (**figure 12.7**). When a zinc atom is converted to a zinc ion in the left compartment, a copper ion changes to a copper atom

Figure 12.7 A simple electrochemical cell. A battery may consist of one or more such cells.



in the right, and a sulfate ion sneaks through the porous plate from the solution in the right compartment to the solution in the left. The charges in the two solutions stay balanced. Why bother with the porous plate? Why not just put both solutions and both electrodes in a single compartment so the sulfate ions don't have to sneak around? If we were to do that, the electrons wouldn't have to make the trip through the wire; they could just be passed from zinc atoms to copper ions, which would now be in contact with one another. And unless the electrons go through the wire, the light bulb won't glow (nor will battery-operated portable radios, hand calculators, or cardiac pacemakers work).

The net reaction for this electrochemical cell is

$$Zn + Cu^{2+} \longrightarrow Zn^{2+} + Cu$$

If 1 *M* solutions of $ZnSO_4$ and $CuSO_4$ are used, the system will produce about 1.1 volts (V) at 25 °C. The volt is a measure of electrical potential, or of the tendency of the electrons in a system to flow.

A battery is technically a series of such cells, the word *battery* meaning a group of similar things (as in a *battery* of tests). The familiar 12-V automobile storage battery consists of six cells wired in series (i.e., one after another), each cell consisting of two electrodes. The cells do not incorporate the zinc-copper couple just described but a somewhat more complicated system involving lead, lead oxide, and sulfuric acid. A distinctive feature of the lead storage battery is its capacity for being recharged. It will supply electricity (i.e., it will discharge) when you turn on the ignition to start the car or when the motor is off and the lights are on. But it can be recharged when the car is moving and an electric current is supplied *to* the battery by the mechanical action of the car (a process we won't detail here).

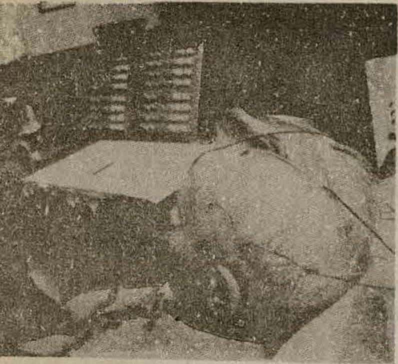


Figure 12.8 An electroencephalogram measures changes in the flow of current associated with the activity of the brain. (Courtesy of Biomedical Graphics, University of Minnesota Hospitals, Minneapolis.)

Ionic processes in and around cells give rise to electrical potentials. These processes are especially important in muscle and nerve cells. Instruments are available which measure small potential differences and small changes in current flow in the human body. The *electrocardiograph* (EKG) monitors the electrical changes associated with the beating of the heart. The *electroencephalograph* (EEG) measures the electrical activity of the brain. The EEG can be connected to the scalp by means of electrodes. The EKG is connected to the body through a suspension of electrolyte on the skin. The changes in current flow associated with the heart's activity are conducted to the EKG through the electrolyte.

12.7 Precipitation: Let It All Fall Out

We have thus far focused our attention on strong electrolytes, those compounds that supply high concentrations of ions in solution. There are ionic compounds whose solubility in water is quite low. For example, the solubility of barium sulfate ($BaSO_4$) is 0.0002 g per 100 g of water at 25 °C. This makes barium sulfate a very weak electrolyte in aqueous solution. The fact that a salt is a weak electrolyte or a nonelectrolyte does not necessarily mean that it is unimportant in the chemistry of living systems. On the contrary, for some physiological processes, the relative insolubility of certain salts is of critical importance. To understand these processes, it will be necessary to consider first a new way of describing solubility, or, more correctly, of determining when a salt will start precipitating from solution because its solubility has been exceeded.

When solid barium sulfate is added to water, an equilibrium is established between the undissolved solute and the ions.

$$BaSO_4(s) \rightleftharpoons Ba^{2+}(aq) + SO_4^{2-}(aq)$$

An extremely small amount goes into solution. Even though barium salts are quite toxic, large amounts of barium sulfate can be swallowed or given by enema because very little will dissolve in the solutions of the body. Since barium sulfate is opaque to X rays, technicians can use it to outline the stomach or intestines for X-ray photographs (**figure 12.9**). The undissolved barium salt scattered throughout the intestine blocks the X rays. The X-ray film is unexposed in these areas, which, therefore, appear white in the developed negative. The barium sulfate is later voided from the body unchanged.

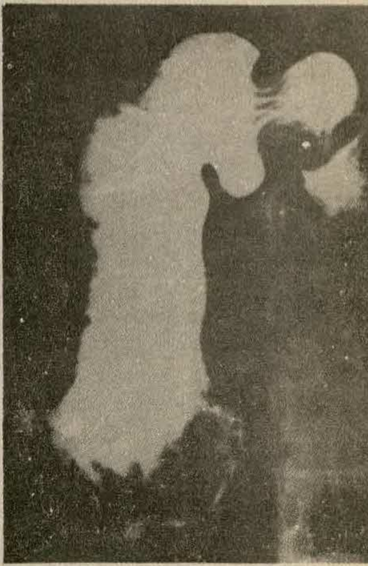


Figure 12.9 Barium sulfate is insoluble in water and opaque to X rays. When swallowed, this salt can be used to outline the stomach for X-ray photographs. (Courtesy of B. Levin, Michael Reese Hospital and Medical Center, Chicago.)

Even though we say that barium sulfate is insoluble, the small amount which does dissolve can be measured (as we indicated above). The concentration of barium ions (Ba^{2+}) and sulfate ions (SO_4^{2-}) in a saturated solution of barium sulfate is 0.00001 *M* (or 1×10^{-5} *M*) each at 18 °C.

The product of the concentrations of the ions in a saturated solution,

$$[Ba^{2+}][SO_4^{2-}]$$

is a constant. At 18 °C, the product is

$$(1 \times 10^{-5})(1 \times 10^{-5}) = 1 \times 10^{-10}$$

This value is called the *solubility product constant* for barium sulfate. It is this constant which we will find useful in predicting whether or not precipitation will occur if a solution containing barium ions is mixed with one containing sulfate ions. Precipitation will occur if the product $[Ba^{2+}][SO_4^{2-}]$ is greater than 1×10^{-10}. Barium sulfate will continue to separate until the product is just equal to 1×10^{-10}. At that value, the solution will be saturated. If the $[Ba^{2+}][SO_4^{2-}]$ is less than 1×10^{-10}, no barium sulfate precipitate will be formed. The solution will be unsaturated in barium sulfate.

As in the case of the ion product of water, K_w (section 11.3), it is the *product* of the ion concentrations which is important. If barium sulfate is simply placed in water, the concentration of barium ion equals the concentration of sulfate ion. It is, however, possible to prepare a solution in which the two concentrations are not equal (example 12.1). The barium ion concentration could be higher than the sulfate ion concentration, or vice versa. Precipitation will always occur when the *product* of the two concentrations exceeds 1×10^{-10}, but precipitation will not necessarily coincide with concentrations of 1×10^{-5} for each ion.

Example 12.1 If 0.001 mole of $BaCl_2$ and 0.0001 mole of Na_2SO_4 are added to 1 *ℓ* of water, will $BaSO_4$ precipitate? (Assume no volume change.)

Table 12.2
Selected solubility product constants at 25 °C

Compound	*Formula*	*Solubility Product Constant*
Silver chloride	$AgCl$	1.2×10^{-10}
Barium sulfate	$BaSO_4$	1.1×10^{-10}
Calcium carbonate	$CaCO_3$	4.8×10^{-9}
Copper(II) sulfide	CuS	8.7×10^{-36}
Mercury(II) sulfide	HgS	3.0×10^{-53}

$BaCl_2$ and Na_2SO_4 are soluble salts; each one will completely dissolve. The 0.001 mole of $BaCl_2$ will yield 0.001 M Ba^{2+} (as well as 0.002 M Cl^-). The 0.0001 mole of Na_2SO_4 will yield 0.0001 M SO_4^{2-} (as well as 0.0002 M Na^+). The product of the barium and sulfate ion concentrations is

$$(0.001)(0.0001) = (1 \times 10^{-3})(1 \times 10^{-4}) = 1 \times 10^{-7}$$

Since 1×10^{-7} is greater than 1×10^{-10},* $BaSO_4$ will precipitate until the product of the $[Ba^{2+}]$ and $[SO_4^{2-}]$ is just equal to 1×10^{-10}. The sodium and chloride ions in solution have no tendency to precipitate as sodium chloride salt, because sodium chloride is quite soluble in water.

The solubility product principle can be used in the preparation of certain compounds. If silver nitrate solution is mixed with sodium chloride solution, slightly soluble silver chloride will precipitate.

$$\underbrace{Ag^+ + NO_3^-}_{\textit{Soluble}} + \underbrace{Na^+ + Cl^-}_{\textit{Soluble}} \longrightarrow \underbrace{AgCl(s)}_{\textit{Insoluble}} + \underbrace{Na^+ + NO_3^-}_{\textit{Soluble}}$$

The silver chloride can be removed by filtration, that is, by pouring the mixture through a porous paper which will trap the solid silver chloride but permit passage of the solution. Further, if equimolar quantities of silver nitrate and sodium chloride are used, the filtrate (the solution going through the filter paper) can be evaporated, and the other ions can be obtained as sodium nitrate in crystalline form. The solubility product of silver chloride, $[Ag^+][Cl^-]$, is equal to 1.6×10^{-10} at 25 °C. That means that a very small number of silver ions and chloride ions in solution will pass through the filter paper. But the vast majority of these ions will be trapped on the paper as the solid salt.

The solubility products for many salts are known. A few values are given in **table 12.2.**

*Remember that the smaller negative exponent corresponds to the larger number. For example, $10^{-1} = 0.1$ and $10^{-2} = 0.01$.

Precipitation is important in the formation of many minerals in nature. Geologists are not the only ones concerned with the formation of mineral deposits, however. Our teeth and bones are largely calcium phosphate salts. One such salt is $Ca_3(PO_4)_2$, sometimes called tricalcium phosphate. Teeth and bones are formed by the precipitation of calcium phosphate salts from solution. In order for this precipitation to occur, the concentrations of ions must exceed the solubility product in the immediate area of deposition. If we assume that the precipitation reaction is

$$3\ Ca^{2+} + 2\ PO_4^{3-} \rightleftharpoons Ca_3(PO_4)_2(s)$$

the solubility product is

$$[Ca^{2+}][Ca^{2+}][Ca^{2+}][PO_4^{3-}][PO_4^{3-}]$$

Each calcium phosphate unit provides three calcium ions (Ca^{2+}) and two phosphate ions (PO_4^{3-}). More simply, we may write the expression as

$$[Ca^{2+}]^3[PO_4^{3-}]^2$$

At a temperature of 37 °C (normal body temperature), the solubility product constant for calcium phosphate is about 4×10^{-27}. In the blood, the concentration of free calcium ions is about 0.0012 *M* (1.2×10^{-3} *M*) and the concentration of phosphate ions is about 1.6×10^{-8} *M*. Plugging these values into the solubility product relationship we get

$$(1.2 \times 10^{-3})^3 \times (1.6 \times 10^{-8})^2 = (1.7 \times 10^{-9})(2.6 \times 10^{-16}) = 4.4 \times 10^{-25}$$

(A brief review on the manipulation of exponential numbers is offered in appendix B.) Since this value is *larger* than the solubility product (4×10^{-27}), we expect precipitation of calcium phosphate and the subsequent growth of bone and tooth to occur.

In growing children, the foregoing description may closely represent the actual mechanism. In adults, however, teeth and bones are no longer growing. What keeps them from getting ever larger? The pH right at the area of growth is a little below 7.4 due to metabolic processes in the cells. Hydronium ions thus produced tie up phosphate ions as hydrogen phosphate ions.

$$PO_4^{3-} + H_3O^+ \rightleftharpoons HPO_4^{2-} + H_2O$$

The phosphate ion concentration is reduced to a value just satisfying the solubility product relationship at the constant value of 4.0×10^{-27}. Normal bone and tooth maintenance takes place, with neither growth nor diminution.

Two pathological conditions of the mouth and teeth are worthy of mention. If the salivary glands are removed or destroyed, the teeth are no longer bathed by saliva. At the usual pH values, saliva provides just the right concentration of calcium ions and phosphate ions to prevent dissolution of the teeth. With the salivary glands gone, the concentration of the ions rapidly falls below the solubility product constant. When this happens, more calcium phosphate dissolves, and the teeth, if not removed, erode away.

A similar situation occurs when children suffer from chronic acidosis. The blood pH may be as low as 7.1, and the pH in the immediate areas of bone formation is probably even lower. Hydronium ions tie up phosphate ions, lowering the concentration of the latter. Bone growth is greatly hindered and the child's skeleton is badly formed.

Tooth decay (caries) can also be related to solubility. A combination carbohydrate-protein called *mucin* forms a film, called plaque, on teeth. If it is not removed by brushing and flossing, buildup of plaque continues. Food and bacteria trapped in the plaque ferment carbohydrates, producing acid. Saliva does not penetrate plaque and hence cannot buffer against the buildup of acid. The pH at the surface of the tooth may go as low as 4.5, and the concentration of phosphate ions in solution is rapidly depleted as hydrogen phosphate ions are formed. The calcium phosphate of the tooth dissolves to replenish the phosphate ion, leaving a cavity in the tooth.

12.8 The Case of the Disappearing Precipitate

In the preceding section, we saw how certain combinations of ions cause precipitates to form. Knowledge of solubility product relationships can also be used to bring slightly soluble salts into solution.

If a relatively concentrated solution of calcium chloride ($CaCl_2$) is added to another with a fair concentration of sodium oxalate ($Na_2C_2O_4$), a precipitate of calcium oxalate (CaC_2O_4) is formed (some kidney stones are primarily calcium oxalate).

$$\underbrace{Ca^{2+} + 2\ Cl^-}_{\textit{Soluble}} + \underbrace{2\ Na^+ + C_2O_4^{2-}}_{\textit{Soluble}} \longrightarrow \underbrace{CaC_2O_4(s)}_{\textit{Insoluble}} + \underbrace{2\ Na^+ + 2\ Cl^-}_{\textit{Soluble}}$$

If hydrochloric acid is now added to the precipitate, the precipitate disappears. The solid dissolves because the oxalate ions ($C_2O_4^{2-}$) are tied up by the hydronium ions (from the HCl) to form soluble, slightly ionized oxalic acid.

$$C_2O_4^{2-} + 2\ H_3O^+ \rightleftharpoons H_2C_2O_4 + 2\ H_2O$$

This decreases the concentration of oxalate ion so that the solubility product constant for calcium oxalate is no longer exceeded. The precipitate dissolves.

Other precipitates can be dissolved by reactions which form slightly soluble gases. Zinc sulfide is ever so slightly soluble in water.

$$ZnS(s) \rightleftharpoons Zn^{2+} + S^{2-}$$

The product of ion concentrations at equilibrium is

$$[Zn^{2+}][S^{2-}] = 1.1 \times 10^{-21}$$

Zinc sulfide dissolves in **hydrochloric acid**, however, because the hydronium ions react with sulfide ions (S^{2-}) to form hydrogen sulfide, which escapes as a gas.

$$S^{2-} + 2\ H_3O^+ \longrightarrow H_2S(g) + 2\ H_2O$$

Removal of sulfide ion soon leads to a situation in which the solubility product constant is no longer exceeded, and the precipitate dissolves.

Unfortunately, strong hydrochloric acid solutions can't be used to dissolve kidney stones from kidneys. The acid would be much too corrosive to our cells. There are chemicals, though, which have shown modest success in dissolving kidney stones. If the stones are calcium oxalate, removing foods containing oxalates from the diet might be of some help.

12.9 The Salts of Life: Minerals

A variety of inorganic compounds are necessary for the proper growth and repair of our tissues. It is estimated that such minerals represent about 4% of human body weight. Some of these, such as the chlorides (Cl^-), phosphates (PO_4^{3-}), bicarbonates (HCO_3^-), and sulfates (SO_4^{2-}), occur in the blood and other body fluids. Others, such as iron (as Fe^{2+}) in hemoglobin and phosphorus in the nucleic acids (DNA and RNA), are constituents of very complex organic compounds.

Minerals essential to one or more living organisms contain the elements sodium (Na), magnesium (Mg), potassium (K), phosphorus (P), sulfur (S), chlorine (Cl), calcium (Ca), manganese (Mn), iron (Fe), copper (Cu), cobalt (Co), zinc (Zn), iodine (I), fluorine (F), silicon (Si), tin (Sn), vanadium (V), chromium (Cr), selenium (Se), molybdenum (Mo), and arsenic (As). These, with the structural elements carbon, hydrogen, nitrogen, and oxygen make up the 25 chemical elements of life. Other elements are sometimes found in body fluids and tissues but are not known to be essential. These include aluminum (Al), lithium (Li), nickel (Ni), and boron (B). It might yet be discovered that one or more of these is essential.

These minerals serve a variety of functions. Perhaps the most dramatic is that of iodine. A small amount of iodine is necessary to the proper function of the thyroid gland. A deficiency of iodine produces dire effects, of which goiter is perhaps the best known. Iodine is available in seafood. To guard against iodine deficiency, a small amount of sodium iodide (NaI) is added to table salt (NaCl). Iodized salt has greatly reduced the incidence of goiter.

Iron(II) ions (Fe^{2+}) are necessary for the proper function of the oxygen-transporting compound hemoglobin. Without sufficient iron, there will be a shortage of oxygen supplied to the body tissues. The resulting weakened condition is called anemia. Foods especially rich in iron compounds include red meats and liver.

As we have seen, calcium and phosphorus are necessary for the proper development of bones and teeth. Growing children need about 1.5 g of each per day. These elements are available in plentiful quantities in milk. The need of adults for these elements is less widely known but very real. For example, calcium ions are necessary for the coagulation of blood (to stop bleeding) and for maintaining the rhythm of the heartbeat. Phosphorus is necessary in order for the body to metabolize carbohydrates (chapter 30). Without phosphorus compounds, we couldn't get *any* energy from those "quick energy" foods. Compounds containing phosphorus play many other essential roles, also. We will encounter a number of these compounds in subsequent chapters.

Sodium chloride in moderate amounts is essential to life. It is important in the exchange of fluids between cells and plasma, for example. The presence of salt increases water retention. A high volume of retained fluids can cause swelling and high blood pressure (hypertension). There are an estimated 23 000 000 people in the United States suffering from hypertension. And most physicians agree that our diets generally contain too much salt.

Iron, copper, zinc, cobalt, manganese, molybdenum, calcium, and magnesium are essential to the proper functioning of certain enzymes. These metallo-enzymes are necessary to life. The functions of some other minerals are quite complex. Some things are known about how they operate, but a great deal remains to be learned about the role of inorganic chemicals in our bodies. Bioinorganic chemistry is a flourishing area of research.

Problems

1. Define or illustrate these terms.
   - a. cathode
   - b. anode
   - c. cation
   - d. anion
   - e. electrolysis
   - f. strong electrolyte
   - g. weak electrolyte
   - h. nonelectrolyte
   - i. ionization
   - j. ion dissociation
   - k. solubility product constant
2. Classify the following as strong electrolytes, weak electrolytes, or nonelectrolytes in solution.
   - a. KCl
   - b. HNO_3
   - c. H_2CO_3
   - d. Na_2SO_4
   - e. KOH
   - f. CH_3OH
   - g. AgCl
   - h. CCl_4
   - i. $CaCl_2$
3. Why does a solution of 1 mole of NaCl in 1 kg of water freeze at a lower temperature than a solution of 1 mole of sugar in 1 kg of water? Why is the freezing-point depression for the salt solution not quite twice that for the sugar solution?
4. Hydrogen chloride is a covalent molecule. Why does a solution of the gas in water conduct electricity?
5. What new substances would be formed if electricity were passed through the following?
   - a. molten KBr
   - b. molten LiCl
   - c. molten Al_2O_3
6. Both $Ba(OH)_2$ and H_2SO_4 are strong electrolytes. When equimolar solutions of the two are mixed, the resulting solution is essentially nonconducting. Write the equation for the reaction and explain the observations.
7. The solubility product constant for $MgCO_3$ is about 1×10^{-5} at 25 °C. Will a precipitate form if 0.001 mole of $MgCl_2$ and 0.001 mole of Na_2CO_3 are added to 1 *l* of water? The *net* ionic reaction is

$$Mg^{2+} + CO_3^{2-} \rightleftharpoons MgCO_3(s)$$

8. Would an object to be electroplated be made the anode or the cathode in an electrolytic cell? Why?
9. If a concentrated solution of sodium acetate is mixed with a solution of silver nitrate a precipitate of silver acetate is formed. The precipitate dissolves readily when nitric acid is added. Write equations to explain what happens.
10. Boiler scale ($CaCO_3$) is insoluble in water, yet it readily dissolves in hydrochloric acid. Write the equation that explains what happens.
11. List five ions important to our body chemistry and explain the role of each.

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chapter 13

Bioinorganic Chemistry

It almost seems a contradiction of terms. *Inorganic* means nonliving and not derived from life. *Organic* means living, having the characteristics of life, or derived from life. At least, those are the everyday definitions of the terms. So how could inorganic chemicals be important to living organisms?

In the old days, chemists used the terms *organic* and *inorganic* in much the same way as everyone else. They believed that, while they could make many different inorganic chemicals, they could not hope to make organic compounds in the laboratory. They believed, with everyone else, that only living organisms, within their tissues, could make organic compounds. Some *vital force*, they thought, was necessary for the synthesis of organic substances.

A series of experiments in the early 1800s led to the overthrow of the vital force theory. Perhaps the most important single step was made by the young German chemist Friedrich Wöhler in 1828. Wöhler made some urea (NH_2CONH_2), long recognized as a typical organic compound, simply by heating a solution of ammonium cyanate ($NH_4^+CNO^-$), a compound generally regarded to be inorganic. Although a few die-hard vitalists held out for several decades, the vital force theory was practically dead by the middle of the 19th century. *Organic chemistry* is now defined as the chemistry of the compounds of carbon. *Inorganic chemistry* is that of all the other elements. Several later chapters will be devoted to organic chemistry. In this chapter we will study some important inorganic chemistry. The elements and their compounds will be organized by family or group, following the periodic table.

13.1 The Noblest Gases of Them All

When Dmitri Mendeléev presented the periodic chart in 1869 (chapter 2), he confidently left spaces in it for elements which he felt should exist but which had yet to be discovered. In succeeding years, his predictions were substantiated by the isolation and identification of the missing elements. In

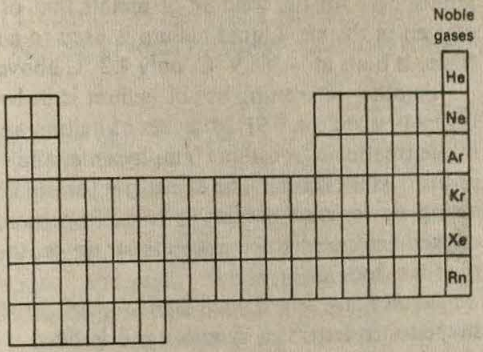


Figure 13.1 The noble gases.

the last decade of the 19th century, however, a series of elements were discovered which made up an entirely new family, one completely unexpected by Mendeléev and his contemporaries. Nonetheless, this new group, called the noble gases, fit neatly between the very reactive alkali metals (Group IA) and the highly active nonmetals of Group VIIA. In the usual flat form of the periodic table, the noble gases are placed to the far right, in the column immediately following Group VIIA.

The six noble gases are helium, neon, argon, krypton, xenon, and radon. All, with the exception of radioactive radon, are components of the atmosphere (**table 13.1**). Argon is rather abundant, making up nearly 1% by volume of the atmosphere. Xenon, on the other hand, is quite rare, making up only 1 part in 11 000 000 of the atmosphere.

Helium is found in natural gas deposits, particularly those under the Great Plains of the United States. Presumably, this helium was formed by the *alpha* decay of radioactive elements within the earth. *Alpha* particles (helium nuclei) become helium atoms by acquiring two electrons. Although some helium is continually being made in the earth's interior, the process is very slow. The helium we tap has been accumulated over eons and, therefore, must be regarded as an essentially nonrenewable resource. Our future supplies are threatened, because it is not economical at present to collect and store all that is produced in commercial operations. Much helium is simply released into the atmosphere.

Helium is used to fill balloons and dirigibles. Its lifting power is more than 90% that of hydrogen, the lightest of all the gases, and helium has the advantage of being nonflammable. Helium is also used to provide an inert

Figure 13.2 The helium-filled Goodyear blimp is a familiar sight to those who watch sports events on television. (Courtesy of Goodyear Tire and Rubber Company, Akron, Ohio.)

Table 13.1
Noble gases in the atmosphere

Gas	*Number of Atoms in 11 000 000 Molecules of Air*
Helium	55
Neon	15
Argon	100 000
Krypton	11
Xenon	1

atmosphere for the welding of metals that otherwise might be attacked by oxygen in the air. Liquid helium is used to achieve extremely low temperatures. It boils at −268.9 °C, only 4.2 °C above absolute zero.

Another interesting use of helium is in breathing mixtures for deep-sea divers (see section 6.9). Mixtures of helium and oxygen have also been used in the treatment of asthma, emphysema, and other conditions involving respiratory obstruction. The same low formula weight which gives helium its lifting power also permits it to diffuse more rapidly than nitrogen. The oxygen-helium mixture puts less strain on the muscles involved in breathing than does air.

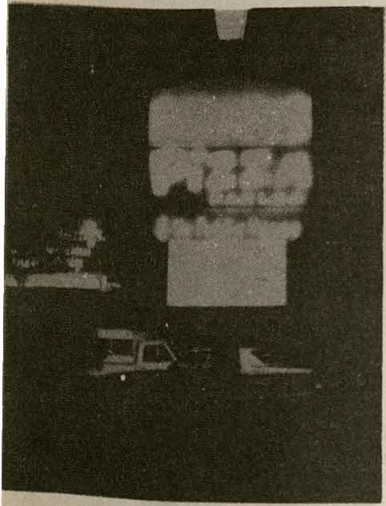


Figure 13.3 The color of neon signs is due to changes in electronic energy levels in neon atoms. (Photo by Mari Ansari.)

Neon is used in lighted signs for advertising. A tube with electrodes is shaped into letters or symbols and is filled with neon at low pressure. An electric current is passed through the tube, causing the atoms to emit their characteristic spectral lines (section 2.10). With a spectroscope, we would see the individual lines. With the unaided eye, however, we merely see the familiar orange-red glow. Other colors are obtained with mixtures of argon and neon or mercury vapor and neon or by use of colored glass for the tube.

Argon, as **table 13.1** shows, is the most plentiful of the noble gases. It can be separated from air rather inexpensively. Argon is used to fill incandescent light bulbs. Unlike nitrogen and oxygen, it does not react with the tungsten filament. It also decreases the tendency of the filament to vaporize, thus extending the filament's life. Fluorescent lights are filled with a mixture of argon and mercury vapor. Argon also provides an inert atmosphere for carrying out chemical reactions in which one or more of the reactants is sensitive to air oxidation.

Krypton and xenon are too expensive to have many important commercial applications, although krypton has found some use in light bulbs. Radon, although exceedingly rare in the atmosphere, can be collected from the radioactive decay of radium.

$$^{226}_{88}\mathrm{Ra} \longrightarrow {}^{4}_{2}\mathrm{He} + {}^{222}_{86}\mathrm{Rn}$$

This radon may be sealed in small vials and used for radiation therapy of certain malignancies.

The noble gases are exceptionally resistant to chemical reaction. Other elements undergo reactions in order to achieve the more stable electronic configurations of the noble gases (chapter 4). All the noble gases exist in elemental form as monatomic species. The other gases we have encountered, such as hydrogen (H_2), nitrogen (N_2), and chlorine (Cl_2), exist as diatomic molecules so that each atom can achieve a stable outer electron configuration, but the individual atoms of the noble gases already have this arrangement. Because of their stability, the noble gases were often called "inert gases." But, in 1962, it was discovered that a few compounds of krypton and xenon could be formed, necessitating the change from "inert" to "noble." (Presumably, radon also would form compounds, but it is relatively rare and highly radioactive. The dangers involved in working with this compound have restricted research involving it.) The first binary (two-element) compound of a noble gas was prepared at Argonne National Laboratory by the simple procedure of heating a mixture of xenon and fluorine (the most reactive element) at 400 °C. Colorless crystals of xenon tetrafluoride (XeF_4) were obtained (**figure 13.4**).

$$Xe(g) + 2\,F_2(g) \longrightarrow XeF_4(s)$$

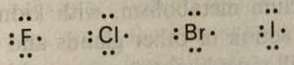
The xenon tetrafluoride crystals are stable at room temperature. In subsequent years, more than 20 compounds of xenon and krypton have been made. As yet, despite many attempts, no compounds have been made of the lighter elements, helium, neon, and argon. While this family of elements is no longer called "inert," its nobility is still unquestioned. More than any other family, the noble gases disdain interactions with the masses of other elements.

Figure 13.4 Crystals of xenon tetrafluoride, the first binary compound of a noble gas. (Courtesy of Argonne National Laboratory, Argonne, Ill.)

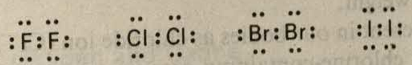
13.2 The Salt Formers: Group VIIA

Fluorine, chlorine, bromine, iodine, and astatine make up Group VIIA, a family of elements called the halogens. We saw in chapter 4 that sodium reacts with chlorine to form sodium chloride, the familiar table salt. Indeed, it is characteristic of the entire group that they react with metals to form salts. The word *halogen* is derived from Greek words meaning "salt former." We will limit our discussion to the first four halogens, for the fifth, astatine, is rare and highly radioactive.

Each halogen atom has seven electrons in its outer energy level, or shell. Their electron dot structures differ only in the central symbol.



All, in the elemental form, exist as diatomic molecules, formed by the sharing of a pair of electrons.



Note that each atom in the molecule has eight electrons in its valence shell, giving it a noble gas configuration.

Another way halogen atoms can achieve a noble gas configuration is by gaining an electron to form a negative ion.

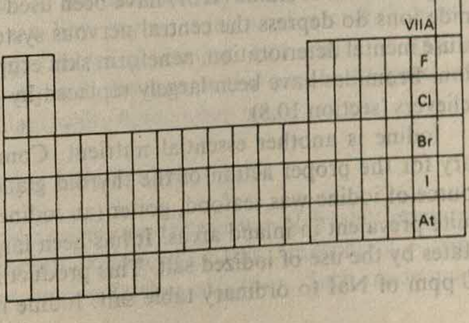


Figure 13.5 Group VIIA, the halogens.

$$:\overset{..}{\underset{..}{F}}\cdot + e^{-} \longrightarrow [:\overset{..}{\underset{..}{F}}:]^{-}$$

This tendency, combined with that of many metals to give up electrons readily, is responsible for the ability of the halogens to form so many salts.

Fluoride salts, in moderate to high concentrations, are acute poisons. Indeed, sodium fluoride (NaF) is used as a poison against such pests as roaches and rats. Small amounts of fluoride ion, however, are essential for our well-being. Up to a point, the hardness of our tooth enamel can be correlated with the amount of fluoride present. Concentrations of 0.7 to 1.0 ppm, by weight, of fluoride (usually as H_2SiF_6 or Na_2SiF_6) have been added to the drinking water of many communities. Evidence indicates that such fluoridation results in a reduction in the incidence of dental caries (cavities) by as much as 50% in some areas. Interpretation of the statistics is complicated, however, by the varying occurrence of fluorides in the diet and by the fact that people retain fluorides at remarkably different rates. One thing that you don't have to worry about is acute poisoning from fluoridated drinking water. You would have to drink 4000 ℓ (1000 gal) of water containing 1.0 ppm of fluoride to approach the lethal dose of 4 g. And that 4000 ℓ would have to be consumed in a fairly short period of time.

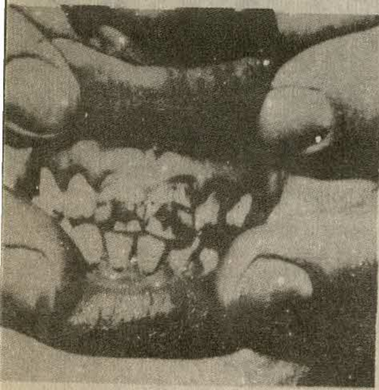


Figure 13.6 Excessive fluoride consumption can cause mottling of tooth enamel. (Courtesy of the National Institutes of Health, Washington, D.C.)

There is some concern about cumulative effects of consuming fluorides in drinking water, in the diet, in toothpastes, and from other sources. Excessive fluoride consumption can cause mottling of the tooth enamel. The enamel becomes brittle in certain areas and gradually discolors. Fluorides also interfere with calcium metabolism, with kidney action, with thyroid function, and with the action of other glands and organs. Fluoridation of public water supplies will most likely remain a subject of controversy.

Chlorine, in the elemental form (Cl_2), is used to kill bacteria in water treatment plants. Sodium hypochlorite (NaOCl) is an ingredient of common household bleaching solutions. Most of these, regardless of price, contain 4.25% NaOCl by weight.

Chlorine is present in our bodies as chloride ion (Cl^-). This ion is essential to life. Many chlorine-containing organic compounds, though, are destructive of life. These include insecticides, herbicides, and even war gases such as phosgene. We will discuss a variety of these compounds in chapter 15.

Several compounds of bromine are of importance. Silver bromide (AgBr) is sensitive to light and is used in photographic film. Sodium bromide (NaBr) and potassium bromide (KBr) have been used medicinally as sedatives. Bromide ions do depress the central nervous system, but prolonged intake can cause mental deterioration, acneform skin eruptions, and, possibly, habituation. Bromides have been largely replaced by other, presumably safer, pain relievers (section 10.8).

Iodine is another essential nutrient. Compounds of iodine are necessary for the proper action of the thyroid gland. Because the major dietary source of iodine was seafood, goiter (an iodine-deficiency disease) was once quite prevalent in inland areas. It has been largely eradicated in the United States by the use of iodized salt. This product is made by addition of about 10 ppm of NaI to ordinary table salt. Iodine is also used as a topical anti-

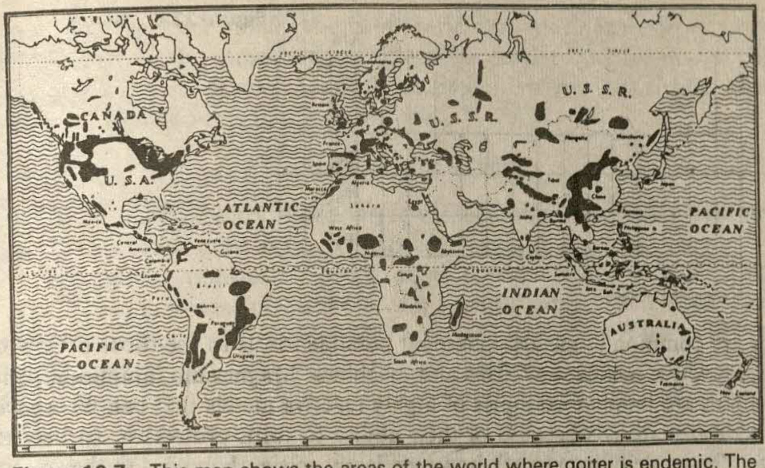


Figure 13.7 This map shows the areas of the world where goiter is endemic. The addition of sodium iodide or potassium iodide to table salt has largely eradicated goiter in the United States.

septic. Tincture of iodine is a solution of elemental iodine (I_2) in a mixture of alcohol and water.

The halogens also react with hydrogen to form the hydrogen halides. In water solutions, these compounds are referred to as the hydrohalic acids. Hydrochloric acid is an example of a hydrohalic acid. These acids are classified as strong, and concentrated solutions are corrosive to tissue. The gaseous hydrogen halides can have disastrous effects on the respiratory system if they occur in significant concentration in the atmosphere. Hydrogen fluoride will etch glass and is used to achieve the decorative frosted designs on some glassware. This same property, however, requires that solutions of hydrogen fluoride not be stored in glass containers. Hydrochloric acid, as we have previously indicated, is present in the stomach and is involved in the digestive process.

13.3 Group VIA: Oxygen and Ozone

Group VIA includes oxygen, sulfur, selenium, tellurium, and polonium. The most important of these is oxygen, which we will discuss in this section. Second in importance is sulfur. We will discuss that element and some of its compounds in section 13.4.

The element oxygen occurs in the atmosphere mainly as the diatomic molecule O_2. In chapter 8, we saw how oxygen is involved in oxidation processes such as combustion (rapid burning), rusting, and corrosion and in respiration. Oxygen reacts rapidly with the more active metals. Magnesium, for example, burns with a brilliant white flame when ignited in air.

$$2\,\mathrm{Mg} + \mathrm{O_2} \rightarrow 2\,\mathrm{MgO} + \text{heat} + \text{light}$$

At room temperature, a reaction occurs on the surface of freshly prepared magnesium metal. This magnesium oxide forms a thin, transparent coating which is impervious to air, preventing further oxidation. Such oxide coat-

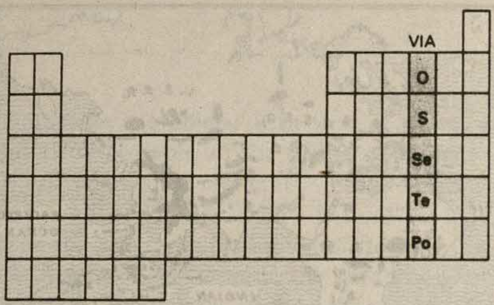


Figure 13.8 Group VIA.

ings are common in metals, making it possible for us to use those otherwise quite reactive metals in utensils and machines. Magnesium, aluminum, and titanium are familiar examples of highly reactive metals that can be used as structural materials because of their ability to form protective oxide coatings. The oxide of iron (rust), however, is not so tightly bound to the surface of the original metal, and it flakes off. This permits the freshly exposed surface to come into contact with more oxygen so that the rusting process can continue until the structure is completely eroded.

Metallic oxides generally form basic solutions when dissolved in water. Barium oxide, for example, reacts with water to form barium hydroxide.

$$BaO(s) + H_2O \longrightarrow Ba(OH)_2(aq)$$

Lithium oxide reacts with water to form lithium hydroxide.

$$Li_2O(s) + H_2O \longrightarrow 2\ LiOH(aq)$$

Generally, oxygen reacts with metals by acquiring electrons and forming oxide ions.

$$O_2(g) + 4\ e^- \longrightarrow 2\ O^{2-}$$

The oxide ions react with water to form hydroxide ions.

$$O^{2-} + H_2O \longrightarrow 2\ OH^-$$

Oxides of metals, then, are generally *basic oxides*.

Oxygen also reacts with many nonmetals. Sulfur, for example, burns in air to form sulfur dioxide.

$$S(g) + O_2(g) \longrightarrow SO_2(g)$$

When dissolved in water, sulfur dioxide reacts to form sulfurous acid.

$$SO_2(g) + H_2O \longrightarrow H_2SO_3(aq)$$

Generally, the oxides of nonmetals form acidic solutions; thus, we call them *acidic oxides*.

Small amounts of oxygen occur as ozone (O_3), an allotropic form of oxygen. *Allotropes* are modifications of an element which can exist in more than one form in the same physical state. (See section 13.7 for one of the more interesting sets of allotropes.) Ozone is quite unstable. At room temperature it breaks down to ordinary oxygen.

$$2\ O_3(g) \longrightarrow 3\ O_2(g) + \text{heat}$$

Ozone is formed by electrical discharges through oxygen and by ultraviolet lamps. The sweetish odor around electrical equipment is due to ozone.

In the upper atmosphere, ozone exists in equilibrium with diatomic oxygen. There it serves to shield us from harmful ultraviolet radiation by absorbing much of the ultraviolet light produced by the sun. The small percentage of ultraviolet light which escapes interaction with ozone is still sufficiently strong to give you a bad case of sunburn. You can imagine the effect on life if the ozone were not there to protect us. Some recent laboratory studies have suggested that many of the compounds used as propellants in aerosol spray cans (spray deodorants, spray waxes, hair sprays, and so on) may react with ozone. If these materials were to reach the upper atmosphere, the ozone layer could be seriously depleted, according to some scientists. The propellant compounds are discussed in chapter 15.

When it occurs near the surface of the earth, ozone is a harmful pollutant, for it is quite toxic. Ozone is formed as a component of photochemical smog (section 13.6). At low concentrations, ozone causes eye irritation. At high concentrations, it may cause pulmonary edema, hemorrhage, and even death. The long-term effects of exposure to low levels of ozone are more difficult to evaluate. Inhalation of ozone and other oxidants* is particularly dangerous during vigorous physical activity. Members of a New Jersey high school football team had to be hospitalized after collapsing during a severe pollution episode. School children in Los Angeles are not allowed to play outside when oxidants reach dangerous levels—as they often do. At concentrations as low as 0.15 ppm oxidants cause damage to vegetation within an hour. Exposure of animals to 1 ppm of ozone for 8 hours a day for a year has produced in them bronchial inflammation and irritation of fibrous tissues. It is not known whether or not the same thing occurs in humans. It is known that oxidant levels have occasionally reached 0.5 ppm in southern California. Levels of 0.15 ppm are frequently exceeded.

In addition to adversely affecting health, ozone causes economic damage. It causes rubber to harden and crack. This shortens the life of automobile tires and other rubber items. As suggested in the previous paragraph, ozone causes extensive damage to crops. Tobacco and tomatoes are particularly susceptible.

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*The term *oxidant* is defined experimentally (with reference to air pollution) as any substance that will oxidize iodide ions (I^-) to free iodine (I_2). This lumping of several compounds under the general heading *oxidants* is based on the fact that there is no simple field test that will identify the separate compounds. And besides, the oxidants all exert a similar physiological effect.

13.4 Group VIA: Sulfur, SO_x, and Acid Rain

Sulfur occurs in nature in both the combined and elemental forms. Free sulfur occurs as S_8, a ring of eight atoms. For simplicity, however, sulfur is usually represented in equations only by the letter *S*, just as if it were monatomic.

Sulfur atoms can accept two electrons to form sulfide ions (S^{2-}).

$$S + 2\ e^- \longrightarrow S^{2-}$$

Sulfur gains electrons from the more active metals to form sulfides.

$$Ca(s) + S(s) \longrightarrow CaS(s)$$

$$Zn(s) + S(s) \longrightarrow ZnS(s)$$

Sulfur can also share electrons with other elements. With two hydrogen atoms, it forms hydrogen sulfide (H_2S). Hydrogen sulfide gas is toxic in fairly low concentrations. It is to our advantage, therefore, that it stinks too. The odor is most often described as that of rotten eggs (which is probably not as descriptive as it once was, since fewer people go around smelling rotten eggs these days). The odor will ordinarily drive people from an area where this gas is building up to dangerous levels.

In the sulfides, sulfur has an oxidation number of −2. Sulfur can also have positive oxidation numbers, for example, +4 in sulfur dioxide (SO_2) and +6 in sulfur trioxide (SO_3). Sulfur burns in air to form sulfur dioxide.

$$S(s) + O_2(g) \longrightarrow SO_2(g)$$

The sulfur dioxide may react further with oxygen to form sulfur trioxide.

$$2\ SO_2(g) + O_2(g) \longrightarrow 2\ SO_3(g)$$

The sulfur trioxide can react in turn with water to form sulfuric acid.

$$SO_3(g) + H_2O \longrightarrow H_2SO_4$$

The two sulfur oxides, collectively called SO_x, and sulfuric acid are the major culprits of one type of smog. London smog, so called because of a dreadful pollution episode in that city in 1952, is a mixture of smoke, fog, soot, sulfur oxides, and often sulfuric acid.

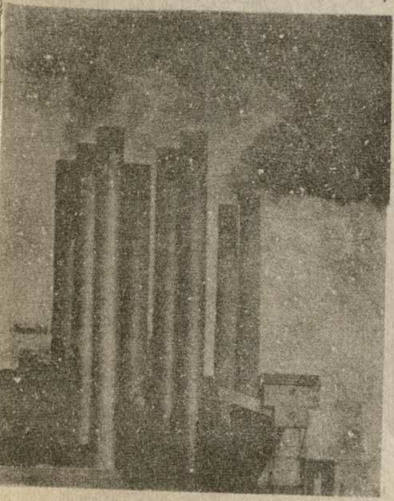


Figure 13.9 A highly visible form of air pollution. (Courtesy of the Minnesota Environmental Control Citizens Association, St. Paul.)

The chemistry of London smog is fairly simple. Coal is mainly carbon, but it contains as much as 3% sulfur, with varying amounts of mineral matter. The sulfur in coal burns, producing acrid, choking sulfur dioxide. It is readily absorbed in the respiratory system, where it serves as a powerful irritant. Sulfur dioxide is known to aggravate the symptoms of people who suffer from asthma, bronchitis, emphysema, and other lung diseases. Sulfuric acid may react with ammonia to form a solid material, ammonium sulfate [$(NH_4)_2SO_4$].

$$2\ NH_3 + H_2SO_4 \longrightarrow (NH_4)_2SO_4$$

The sulfuric acid, in the form of minute liquid droplets, and the finely divided solid ammonium sulfate are easily trapped in the lungs. The harmful effect of these pollutants is considerably magnified by interaction. A particular level of sulfur dioxide, without the presence of particulate matter (finely divided solids), might be reasonably safe. A certain level of particulate matter, without sulfur dioxide around, might be fairly harmless. But take the same levels of the two together, and the effect might well be deadly. An interaction in which the total effect of two ingredients is greater than the sum of the effects of the two ingredients taken separately is *synergistic*. Synergistic effects are quite common whenever chemicals get together. We will encounter synergism again in our study of the action of barbiturate drugs (chapter 19).

As we saw in chapter 10, the oxides of sulfur affect vegetation and other materials in addition to people. Leaves of plants show a bleached, splotchy effect, and both the yield and the quality of crops can be affected by exposure to oxides of sulfur. Rain in industrialized countries has become more acidic in recent years. This increase has been attributed to increased amounts of sulfur oxides released into the atmosphere. Acidic rainwater can corrode metals, eat holes in nylon stockings, and even decompose stone buildings and statuary.

The element sulfur is essential to life. It is found in most proteins, including the enzymes that mediate cellular processes. We will look at the chemistry of organic sulfur compounds in chapter 20. The importance of sulfur in biochemistry will be illustrated many times in subsequent chapters.

13.5 Group VA: Nitrogen Compounds

Group VA includes nitrogen, phosphorus, arsenic, antimony, and bismuth. We will discuss the chemistry of nitrogen and some of its compounds in this section. In section 13.6, we will pay particular attention to the role of nitrogen oxides in air pollution. The element nitrogen occurs as N_2 in the atmosphere. It also occurs in the combined form in nature. It is an essential element, occuring in all proteins and in many other molecules important to living organisms. We will discuss some organic compounds of nitrogen in chapter 19. Biological compounds containing nitrogen atoms will be a major part of our study in subsequent chapters.

Although nitrogen makes up 78% of the atmosphere, the molecules of nitrogen gas cannot be used directly by higher plants or by animals. They

Figure 13.10 Group VA.

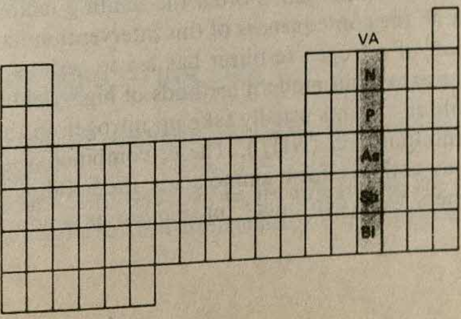
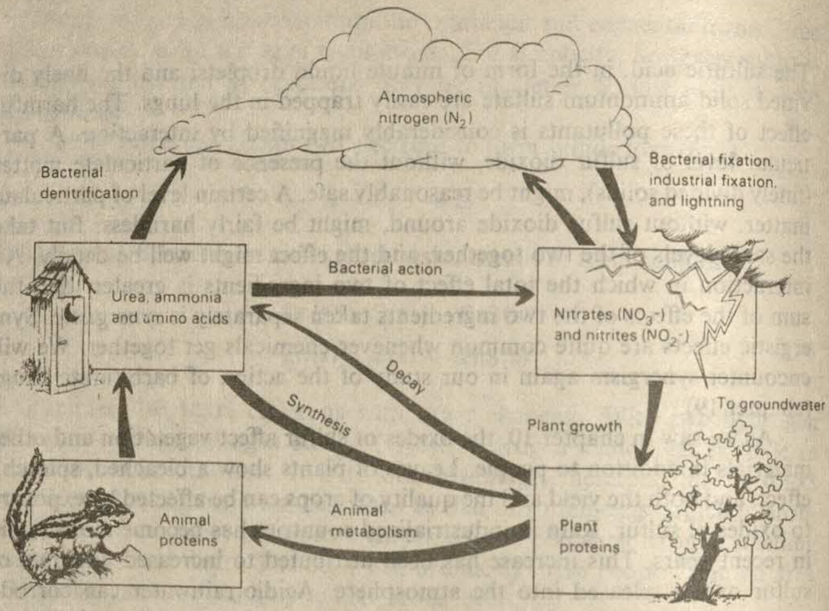


Figure 13.11 The nitrogen cycle.


Atmospheric nitrogen (N_2)
Bacterial denitrification
Bacterial fixation, industrial fixation, and lightning
Bacterial action
Urea, ammonia and amino acids
Nitrates (NO_3^-) and nitrites (NO_2^-)
Decay
Synthesis
To groundwater
Plant growth
Animal proteins
Animal metabolism
Plant proteins

first have to be "fixed," that is, converted to a more readily used form. Certain types of bacteria convert atmospheric nitrogen to nitrates. Other bacteria convert the nitrogen in compounds back to nitrogen gas. A nitrogen cycle (**figure 13.11**) is thus established. Lightning also serves to "fix" nitrogen by causing it to combine with oxygen. Nitric oxide (NO) and nitrogen dioxide (NO_2) are formed. The equations are

$$N_2 + O_2 \xrightarrow{\text{lightning}} 2\,NO$$

$$2\,NO + O_2 \longrightarrow 2\,NO_2$$

The latter reacts with water to form nitric acid (HNO_3).

$$3\,NO_2 + H_2O \longrightarrow 2\,HNO_3 + NO$$

The nitric acid falls in rainwater, adding to the supply of available nitrates in sea and soil. Scientists have undertaken substantial intervention in the nitrogen cycle by industrial fixation—the manufacture of nitrogen fertilizers. This intervention has greatly increased our food supply, for the availability of fixed nitrogen is often the limiting factor in the production of food. Not all the consequences of this intervention have been favorable. Excessive runoff of nitrogen fertilizer has led to serious water pollution problems in some areas, but modern methods of high-yield farming demand "chemical" fertilizers. Plants usually take up nitrogen in the form of nitrates (NO_3^-) or ammonium ion (NH_4^+). These, combined with carbon compounds from photosynthesis, form amino acids, the building blocks of proteins. For years farmers were dependent on manure as a source of nitrates. Discovery of deposits of sodium nitrate, called Chile saltpeter, in the deserts of northern Chile led to exploitation of this substance as a supplemental source of nitrogen. It also led to a bloody war between Bolivia and Chile over these nitrate deposits. The war raged for 4 years (1879–1883). Bolivia lost not only the fertilizer deposits but its outlet to the sea as well.

A rapid rise in population in the late 19th and early 20th centuries led to increasing pressure on the available food supply. This in turn led to an increasing demand for nitrogen fertilizers. The atmosphere offered a seemingly inexhaustible supply—if only it could be converted to a form useful to humans. Every flash of lightning forms some nitric acid in the air. This process probably contributes about 9 kg of nitrogen per hectare of land (about 8 lb per acre). Henry Cavendish duplicated this natural process in 1776 by passing an electric spark through a mixture of nitrogen and oxygen, but little came of this achievement.

The first real breakthrough in nitrogen fixation came in Germany on the eve of the First World War. The process, developed by Fritz Haber, made possible the combination of nitrogen with hydrogen to make ammonia (section 1.1).

$$3\ H_2 + N_2 \rightarrow 2\ NH_3$$

By 1913, one plant was in production and several more were under construction. The Germans were able to make ammonium nitrate (NH_4NO_3), an explosive, by oxidizing part of the ammonia to nitric acid.

$$2\ NH_3 + 4\ O_2 \rightarrow 2\ HNO_3 + 2\ H_2O$$

The nitric acid was then reacted with the rest of the ammonia, and ammonium nitrate was produced.

$$HNO_3 + NH_3 \rightarrow NH_4NO_3$$

The Germans were mainly interested in ammonium nitrate as an explosive, but it turned out to be a valuable nitrogen fertilizer as well. The same discovery that enabled the Germans to prolong World War I probably helped postpone Thomas Malthus' predictions of ghastly famine for several decades.

Increasingly, ammonia is applied directly as fertilizer. A gas at room temperature, ammonia is soluble in water and is also easily compressed into a liquid which can be stored and transported in tanks. Much of it, as we mentioned, is converted to ammonium nitrate, a crystalline solid. Some is converted to solid ammonium sulfate [$(NH_4)_2SO_4$] by reaction with sulfuric acid.

$$2\ NH_3 + H_2SO_4 \rightarrow (NH_4)_2SO_4$$

These may be applied separately or combined with other plant nutrients to make a more complete fertilizer.

It is largely through nitrogen fertilizers that we are able to feed the great human population that inhabits the earth. Unfortunately, our ways of fixing

Fritz Haber was awarded the Nobel Prize for chemistry in 1918. There are a number of ironies in this. Alfred Nobel, a Swedish inventor and chemist who died in 1896, endowed the Nobel Prize (including the peace prize) with a fortune derived from his own work with explosives. During his lifetime, he was bitterly disappointed that the explosives he developed for excavation and mining were put to such disastrous use in wars. And Haber, a man who helped his country during World War I, was exiled from his native land in 1933. He was a Jew. Nazi racial laws forced him out of his position as director of the Kaiser Wilhelm Institute of Physical Chemistry. He accepted a post at Cambridge University in England, but his life was ended by a stroke less than a year later.

nitrogen require great quantities of energy. The petroleum shortages and higher prices of the middle 1970s have led to scarcity and to inflation of fertilizer prices. If only we could find a way to fix nitrogen gas at ambient temperatures, the way microorganisms do . . .

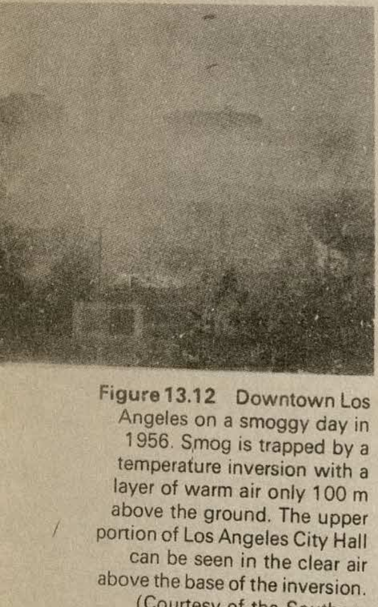


Figure 13.12 Downtown Los Angeles on a smoggy day in 1956. Smog is trapped by a temperature inversion with a layer of warm air only 100 m above the ground. The upper portion of Los Angeles City Hall can be seen in the clear air above the base of the inversion. (Courtesy of the Southern California Air Pollution Control District, Los Angeles.)

13.6 Nitrogen Oxides and Air Pollution

Automobiles also fix nitrogen. Indeed, any time air is subjected to high temperatures, some of the nitrogen and oxygen combine. Unfortunately, most automobiles operate in urban areas, not on farms. And the nitrogen oxides undergo reactions with other pollutants to form a variety of noxious chemicals, not just fertilizers. This type of air pollution is called Los Angeles smog, or, more properly, photochemical smog. In contrast to the London type, which requires cold, damp air, the photochemical type usually occurs in dry sunny climates. The principal culprits are unburned hydrocarbons and oxides of nitrogen from automobiles. The warm, sunny climate that has drawn so many people to the Los Angeles area is also the perfect setting for photochemical smog.

The combustion process in an automobile engine leads to the formation of nitric oxide (NO).

$$N_2 + O_2 \longrightarrow 2\ NO$$

Nitric oxide is oxidized slowly by oxygen to nitrogen dioxide (NO_2).

$$2\ NO + O_2 \longrightarrow 2\ NO_2$$

Nitrogen dioxide is an amber-colored gas. Smarting eyes and a brownish haze are excellent indicators of Los Angeles smog. It is this nitrogen dioxide that plays a vital (villain's) role in photochemical smog. It absorbs a photon of sunlight and breaks down into nitric oxide and very reactive oxygen atoms.

$$NO_2 + \text{sunlight} \longrightarrow NO + O$$

This oxygen atom reacts with other components of the automobile exhaust and the atmosphere to produce a variety of irritating and toxic chemicals (**figure 13.13**).

At concentrations currently found in air, the oxides of nitrogen are not

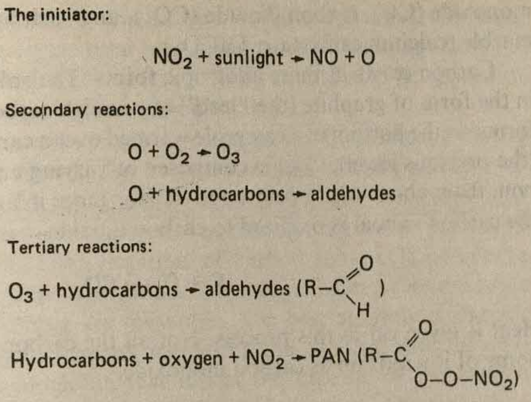

The initiator:
NO_2 + sunlight → NO + O
Secondary reactions:
$O + O_2 \rightarrow O_3$
O + hydrocarbons → aldehydes
Tertiary reactions:
O_3 + hydrocarbons → aldehydes (R–C(=O)H)
Hydrocarbons + oxygen + NO_2 → PAN (R–C(=O)O–O–NO_2)

Figure 13.13 A summary of some of the principal reactions in the formation of photochemical smog. Most reactive intermediates have been omitted from this simplified scheme. For a more complete account see reference 1.

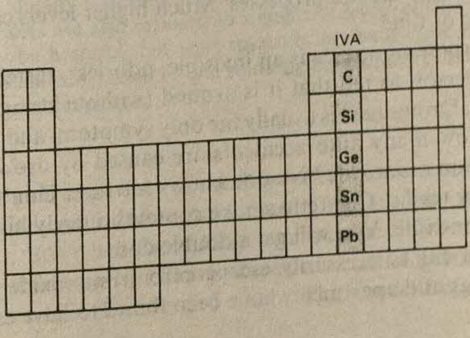
particularly dangerous in themselves. Nitric oxide at high concentrations will react with hemoglobin. As with carbon monoxide, this leads to oxygen deprivation. Such levels are seldom, if ever, reached from ordinary air pollution but might be reached near a specific industrial source. Nitrogen dioxide serves as an irritant to the eyes and respiratory system. Tests with laboratory animals indicate that chronic exposure to levels in the range of 10 to 25 ppm might lead to emphysema or other degenerative diseases of the lungs.

The most serious environmental effect of the nitrogen oxides is their role in smog formation. However, these gases do contribute to the fading and discoloration of fabrics. By forming nitric acid, nitrogen oxides contribute to the acidity of rainwater, accelerating the crorrosion of metals. They also contribute to crop damage, although specific effects are difficult to separate from those of sulfur dioxide and other pollutants.

13.7 Group IVA: Carbon and Some of Its Compounds

Group IVA is made up of carbon, silicon, germanium, tin, and lead. Of these, carbon is easily the most important. Carbon forms thousands—perhaps millions—of compounds with hydrogen. These compounds, called hydrocarbons, will be discussed in detail in the next chapter. Hydrocarbons and their derivatives are called organic chemicals, and their study is called organic chemistry. There are a few simple compounds of carbon, though, that are more like inorganic than organic chemicals. Among these are carbon

Figure 13.14 Group IVA.



monoxide (CO), carbon dioxide (CO_2), and such minerals as limestone and marble (calcium carbonate, $CaCO_3$).

Carbon exists in three allotropic forms. The solid element can be found in the form of graphite (the "lead" of pencils), carbon black (the soot which forms on the bottom of a casserole warmed over a candle flame), and diamond (the precious jewel). Coal is composed of varying amounts of elemental carbon, from about 6% in peat up to 88% or more in anthracite. When burned, the carbon in coal is oxidized to carbon dioxide.

$$C + O_2 \rightarrow CO_2$$

Heat is given off in this process. Not all the carbon is completely oxidized. Some of it winds up as carbon monoxide.

$$2\ C + O_2 \rightarrow 2\ CO$$

Still other carbon, essentially unburned, ends up as soot.

Hydrocarbons are also burned as fuels. Methane, the simplest hydrocarbon, burns with a hot flame. If sufficient oxygen is present, the main products are relatively innocuous carbon dioxide and water.

$$CH_4 + 2\ O_2 \rightarrow CO_2 + 2\ H_2O$$

More complex hydrocarbons are present in gasoline. Let's illustrate the combustion process with an octane, one of the hundreds of hydrocarbons which make up the mixture.

$$2\ C_8H_{18} + 25\ O_2 \rightarrow 18\ H_2O + 16\ CO_2$$

If combustion occurs in sufficient oxygen, the major products are carbon dioxide and water. If insufficient oxygen is present, carbon monoxide is formed. Millions of tons of this invisible but deadly gas are poured into the atmosphere each year, about 80% of it from automobile exhausts. The danger level for carbon monoxide is 10 ppm. Even in off-street urban areas, the level averages 7 to 8 ppm. On the streets of Chicago and Philadelphia, the danger level is exceeded one-third to one-half the time. In Los Angeles, the danger level is topped 40% of the time. Such levels do not cause immediate death, but exposure over a long period of time can cause impairment of the physical and mental processes. Much higher levels can be tolerated for short periods of time.

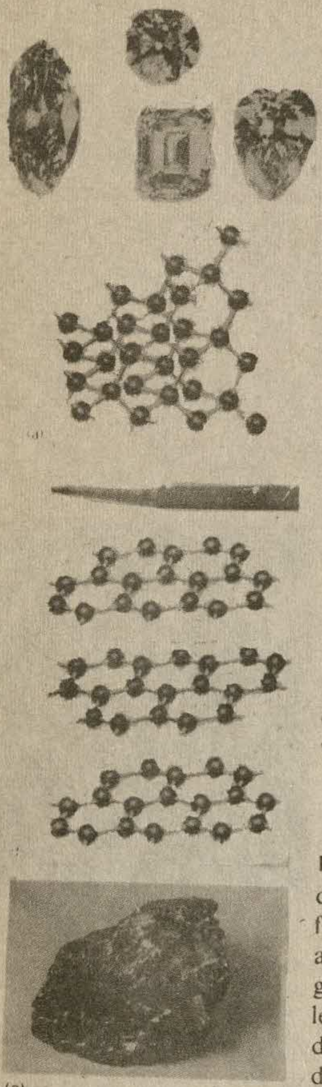


Figure 13.15 The allotropic forms of carbon. (a) Diamond. (b) Graphite. (c) Amorphous. Coal has no regular molecular structure. (Photos and models of diamond and graphite reprinted with permission from Cotton, F. A., Darlington, C. L., and Lynch, L. D., *Chemistry: An Investigative Approach*, rev. ed., Boston: Houghton Mifflin, 1976. Copyright © 1976 by Houghton Mifflin Company. Photo of coal by Dennis Tasa.)

Carbon monoxide is an invisible, odorless, tasteless gas. There is no way for a person to tell that it is around (without using test reagents or instruments). Drowsiness is usually the only symptom, and that is not an unpleasant one. How many auto accidents are caused by drowsiness or sleep induced by carbon monoxide? No one knows for sure. Don't smoke while you drive in heavy traffic. Cigarette smoke contains a fairly high concentration of carbon monoxide. You will get a double dose.

You can't necessarily escape carbon monoxide by going inside. Office buildings and apartments have been found to have essentially the same concentration of carbon monoxide as the air outside. In some areas, this level exceeds federal standards. It has been recommended that buildings in high-traffic areas be tightly sealed at lower levels. They should also be spaced in such a way that the wind can disperse the pollutants.

Carbon monoxide is not an irritant. It exerts its insidious effect by tying up the hemoglobin in the blood. The normal function of hemoglobin is to transport oxygen (**figure 13.16**). Carbon monoxide binds tenaciously to hemoglobin—once on, it refuses to get off. The hemoglobin is thus prevented from transporting oxygen. The symptoms of carbon monoxide poisoning are therefore those of oxygen deprivation. All except the most severe cases of carbon monoxide poisoning are reversible. The best antidote is the administration of pure oxygen. Greatly increasing the concentration of oxygen favors the oxygen-hemoglobin reaction at the expense of the carbon monoxide–hemoglobin combination. Artificial respiration may help if a tank of oxygen is not available.

Carbon monoxide is very much a local pollution problem. It is a severe threat to urban areas with heavy traffic, but it does not appear to be a global threat. In laboratory tests carbon monoxide will survive about 3 years in contact with air. But nature is somehow able to prevent an overall buildup, despite the large amounts being poured into the environment. In fact, it is estimated that up to 80% of the carbon monoxide in the atmosphere comes from natural sources. Except for those highly localized situations (they're bad enough!), nature seems to have the carbon monoxide situation under control.

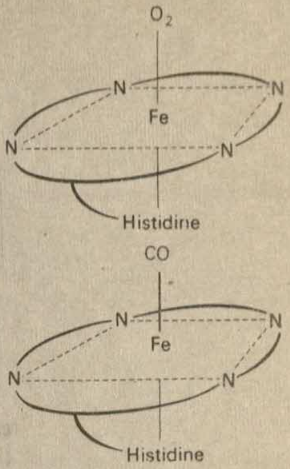


Figure 13.16 Schematic representations of a portion of the hemoglobin molecule. Histidine is an amino acid. Carbon monoxide bonds much more tightly than oxygen.

The Minipolluters: Cigarettes, Smokers, and Nonsmokers. The smoke-filled room is well known in political mythology as the place where decisions are made. The health effects of smoking on the smoker are also widely known. These have been publicized following a series of reports by the Surgeon General. The first report was published in 1964 and led to a ban on television advertisements of cigarettes. The 1972 report (reference 8) included a chapter on the effect of tobacco smoke as an air pollutant. It may well end the era of the smoke-filled room.

A series of studies have shown that the air quality in such a room is very poor. The level of carbon monoxide, even in a well-ventilated room, is often equal to or greater than the legal limits permitted for ambient air quality. These levels have been shown to impair time-interval discrimination. In severe cases, performance on psychomotor tests was impaired. Health effects on people already suffering from heart or lung disease might be quite severe. Nonsmokers are also exposed to significant levels of "tar" and nicotine. These may be harmful, but little research has been done in this area. Some states have already acted to ban smoking in meeting rooms, waiting rooms, and other public places.

Not only is carbon dioxide a product of combustion, it is also produced in respiration. Generally, it is regarded as innocuous. Certainly any immediate effect on us is slight. But what about long-term changes? No matter how "clean" an engine or a factory is, as long as it burns coal or petroleum products, it will produce carbon dioxide and water. The concentration of

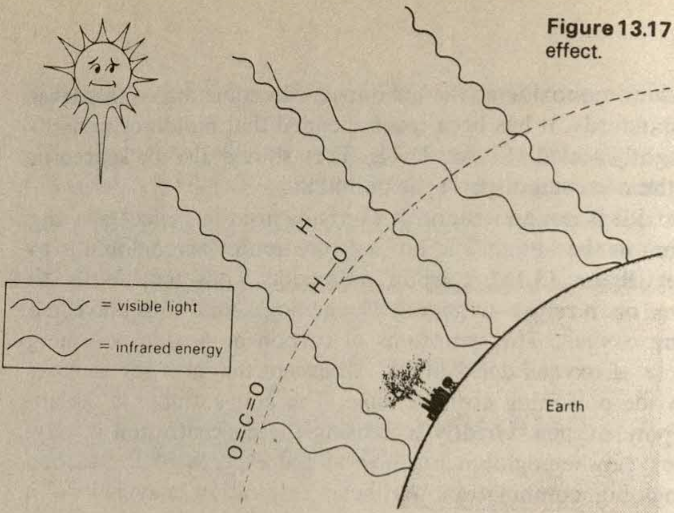


Figure 13.17 The greenhouse effect.

carbon dioxide in the atmosphere has increased 7.5% in this century. It continues to increase at an expanding rate through the increased burning of carbon fuels.

Both water vapor and carbon dioxide produce a "greenhouse effect." These chemicals let the sun's rays (visible light) in to warm the surface of the earth, but when the earth tries to radiate this energy back out into space as heat (infrared energy), the energy is trapped by the molecules of carbon dioxide and water (**figure 13.17**). Water vapor spewed into the atmosphere soon falls back to earth as rain. It therefore affects the climate mostly at the local level. Carbon dioxide poured into the air is not so readily dissipated. It hangs around to affect the climate of the entire world. The concentration of carbon dioxide is now increasing at a rate of 1 ppm per year. Some scientists predict a warming trend which will melt the polar ice caps, thus flooding coastal cities.

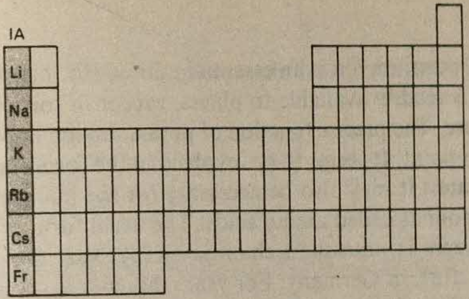
At present the earth's atmosphere seems to be cooling, not warming. We also pour soot, smoke, and dust into the atmosphere. These, perhaps aided by the vapor trails of jet aircraft, screen out the sun's light and tend to lower the earth's temperature. We may not always be so lucky as to balance one effect against another.

13.8 Group IA: The Alkali Family

The Group IA elements are called the alkali metals (from Arabic words describing a source of these elements). Because the hydroxides of these elements are strongly basic, basic solutions are said to be alkaline. There are six elements in the group, lithium (Li), sodium (Na), potassium (K), rubidium (Rb), cesium (Cs), and francium (Fr). The last is highly radioactive, and little is known of its properties. It will not be discussed further here.

In the elemental form, the alkali metals are soft solids with low melting points. Indeed, on a hot day, cesium would be a liquid, for it melts at 29 °C (84 °F). These metals, when freshly cut, are bright and shiny, but they tarnish readily as they become oxidized by the atmosphere. All are highly

Figure 13.18 Group IA, the alkali metals.



reactive, showing a great tendency to give up electrons and form 1+ ions. For example,

$$Na \longrightarrow Na^+ + 1\ e^-$$

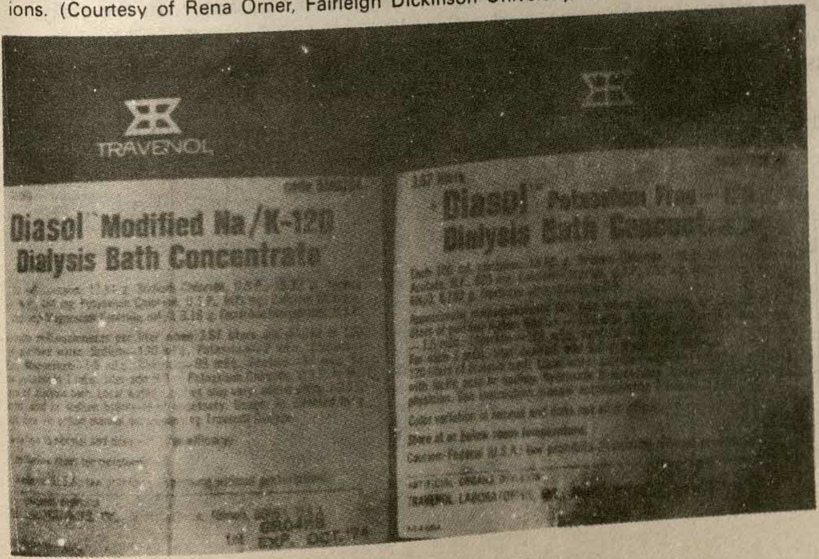
$$K \longrightarrow K^+ + 1\ e^-$$

In compounds, the alkali metals occur almost exclusively as the 1+ ions. A variety of compounds are of considerable importance.

Lithium salts are found in certain naturally occurring brines. Lithium carbonate (Li_2CO_3) is used in medicine to level out the dangerous "manic" highs that occur in manic-depressive psychoses. Some practitioners also recommend lithium carbonate for the depression stage of the cycle. Its mode of action, unfortunately, is still largely unknown.

Sodium salts are quite common. Ordinary table salt (NaCl) supplies the body with chloride ion, necessary for the production of hydrochloric acid by our stomachs. Living tissues require a balance of sodium ion and potassium ion. In animals, the former predominates; in plants, the latter. By salting our vegetables we maintain the proper balance (although it is safe to say that few people have precisely this objective in mind when they pick up the salt shaker).

Figure 13.19 As these dialysate labels indicate, care must be taken to ensure that patients undergoing renal dialysis maintain a proper balance of sodium and potassium ions. (Courtesy of Rena Orner, Fairleigh Dickinson University, Rutherford, N.J.)



Potassium ion is an essential nutrient for plants. It is generally abundant and is readily available to plants, except in soil depleted by high-yield agriculture. The precise function of potassium ion in plant cells has been difficult to pinpoint. It seems to be involved in the formation and transport of carbohydrates. It may also be necessary for the buildup of proteins from smaller compounds called amino acids. The usual form of potassium in commercial fertilizers is potassium chloride (KCl). Vast deposits of this salt occur at Strassfurt, in Germany. For years this source supplied nearly all the world's potassium fertilizer. With the coming of World War I, the United States sought supplies within its own borders. Deposits at Searles Lake, California, and Carlsbad, New Mexico, now supply most of the needs of the United States. Canada has vast deposits in Saskatchewan and Alberta. Beds of potassium chloride up to 200 m (about 700 ft) thick lie about 1 km (0.6 mi) below the prairies.

In animals, potassium ions are the principal positive ions inside cells. There they serve to maintain the osmotic pressure and electrical potential of cells. Sodium ions are the principal positive ions in the extracellular fluid. They are involved in fluid retention and blood pressure. Thus, individuals who are hypertensive or who are suffering from edema are advised to give up salt (NaCl). Sodium ions also serve to regulate the excitability of nerves and muscles. We will discuss these aspects in greater detail in chapter 28.

Many acidic drugs are used in the form of their sodium or potassium salts. These ionic forms are more soluble in water than the "free" acids. For example, benzylpenicillinic acid (free penicillin G) is sparingly soluble in water. The potassium salt (potassium penicillin G) is quite soluble.

We will encounter other sodium and potassium salts in subsequent chapters. Salts of rubidium and cesium, however, are expensive and are rarely encountered.

13.9 Group IIA: The Alkaline Earth Family

The oxides and hydroxides of the Group IIA elements are basic. Only those of the heavier elements are appreciably soluble in water. In the early days of chemistry, the name *earth* referred to substances unaffected by heat and insoluble in water. Now, all of these facts together account for the name assigned to the Group IIA elements, the alkaline earth metals.

The six alkaline earth metals are beryllium, magnesium, calcium, strontium, barium, and radium. In the elemental form, these metals are fairly

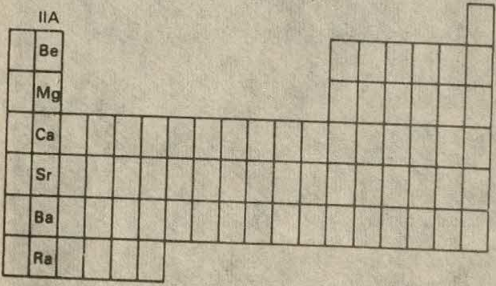


Figure 13.20 Group IIA, the alkaline earth family.

soft and reactive. They show a tendency to give up electrons and form 2+ ions. For example,

$$Mg \longrightarrow Mg^{2+} + 2\,e^-$$

$$Ca \longrightarrow Ca^{2+} + 2\,e^-$$

In compounds, these metals occur almost exclusively as the 2+ ions. Many of the compounds are of great importance.

Beryllium is something of an "oddball" member of the family. Unlike the others, it does not react with water. Indeed, beryllium tends to form covalent, rather than ionic, bonds. The metal itself is rather hard, rigid, and strong. Its lightness makes it quite valuable in structural alloys. The element is poisonous in all its forms. Inhalation of the metal or of beryllium oxide may cause *berylliosis*, a serious and sometimes fatal lung disease which resembles the infamous "black lung" disease of coal miners.

Magnesium ions (Mg^{2+}) are essential to both plants and animals. In plants, magnesium ions are incorporated into chlorophyll molecules. Thus, this ion is essential to photosynthesis. Both calcium and magnesium ions are found primarily within the cells. They are essential for proper functioning of the nerves that control muscles.

Calcium ions are necessary for the proper development of bones and teeth. For this reason, growing children are usually encouraged to drink milk, a rich source of calcium. Adults also require calcium, which is necessary for clotting of blood and maintenance of a regular heartbeat.

Calcium carbonate (limestone) and other rocks containing calcium ions (Ca^{2+}), magnesium ions (Mg^{2+}), or iron ions (Fe^{2+} or Fe^{3+}) are widely distributed in nature. Most compounds containing these ions are only slightly soluble, yet enough of the ions dissolve in the natural water in some areas to cause problems. Water containing calcium, magnesium, or iron ions is what is known as *hard water*. The ions react with the negative ions in soaps to form precipitates. For example,

$$\underset{\textit{Soap}}{Ca^{2+}(aq) + 2\,C_{17}H_{35}COO^-(aq)} \longrightarrow \underset{\textit{Bathtub ring}}{Ca(C_{17}H_{35}COO)_2(s)}$$

This curdy precipitate clings to clothes, hair, and skin, leaving them dingy and dirty in appearance and feel even when they've been freshly washed.

13.10 The B Groups: Some Representative Transition Elements

Most of our attention so far has been focused on the A groups of the periodic table. The chemistry of the B groups is also important, if perhaps more complicated. The B groups, collectively, are called the transition elements. All are metals in the elemental form. They conduct electricity and have characteristic metallic luster.

The transition elements, in general, are those in which *inner* electron shells are being filled. (Group IB and IIB elements are exceptions, yet they share many properties with the other B groups and are often included as transition elements.) Recall from chapter 2 that the third period (or row) of

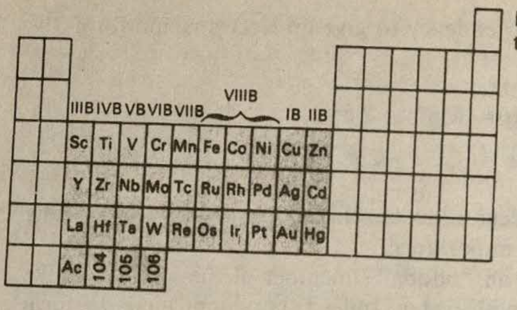

VIIIB
IIIB IVB VB VIB VIIB IB IIB
Sc Ti V Cr Mn Fe Co Ni Cu Zn
Y Zr Nb Mo Tc Ru Rh Pd Ag Cd
La Hf Ta W Re Os Ir Pt Au Hg
Ac 104 105 106

Figure 13.21 The B groups, or the transition elements.

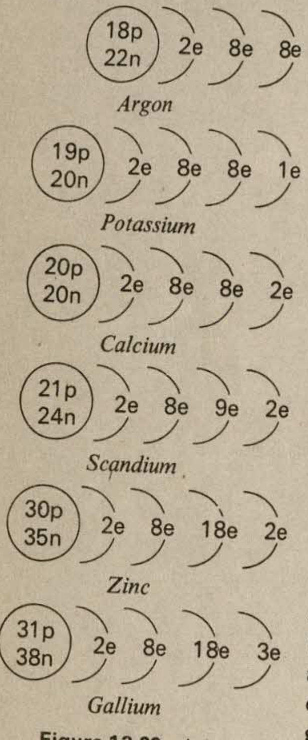


Figure 13.22 It is in the transition elements that inner electron shells begin to be filled to capacity.

the periodic table ended with argon, which has 8 electrons in its outermost shell (**figure 13.22**). The fourth period begins with potassium, which has 1 electron in its fourth shell. The next element, calcium, has 2 electrons in its fourth shell. Recall, however, that the $2n^2$ rule (introduced in section 2.10) predicts a maximum of 18, not 8, electrons for the third shell ($2n^2 = 2 \times 3^2 = 2 \times 9 = 18$). The fourth shell has begun to fill before the third one is full. Things return to "normal" with the next element, scandium. This element skips back and continues to fill the third shell. The first transition series (from scandium to zinc) corresponds to a completion of the filling of the third shell with up to its maximum capacity of 18 electrons. Zinc has the structure represented in **figure 13.22.** With gallium (Ga), whose atomic number is 31, we return to an A group element. All inner shells are filled and the next electron enters the outer shell.

Physical properties vary widely in the transition series. For example, mercury (Hg) is a liquid at room temperature (its melting point is −38 °C). Tungsten (W), however, melts at 3410 °C. Chemically, the elements also exhibit a variety of properties. Most exist in more than one oxidation state in compounds. Iron is a familiar example. It readily forms both iron(II) and iron(III) ions. Some important transition elements are listed in **table 13.2.**

Many compounds of the transition metals are colored, often brilliantly so. The color varies with the oxidation state of the metal in the compound. An aqueous solution containing manganese ions (Mn^{2+}) is a faint pink. Solutions of MnO_4^{2-} (in which the oxidation number of manganese is +6) are an intense green, and those of MnO_4^- (in which the oxidation number of manganese is +7) are deep purple. Aqueous solutions of Fe^{2+} are pale green; those of Fe^{3+} are yellow.

Transition metals known to be essential to life are iron, copper, zinc, cobalt, manganese, vanadium, chromium, and molybdenum. Nickel is sometimes found in body tissues but has not been shown to be essential. Other transition metals, most notably cadmium and mercury, are dangerous poisons.

Iron is essential for the proper functioning of hemoglobin, the red protein molecule involved in oxygen transport. This iron must be in the +2 oxidation state. If it is oxidized to the +3 state, the resulting compound (called methemoglobin) is incapable of carrying oxygen. The resulting oxygen-deficiency disease is called methemoglobinemia. In infants, this condition is called the blue-baby syndrome.

Table 13.2
Some properties of representative transition elements

Element	*Symbol*	*Electronic Configuration*	*Common Oxidation Numbers*	*Melting Point (in degrees Celsius)*	*Density (in grams per millilitre)*
Vanadium	V	2 8 11 2	2+, 3+, 4+, 5+	1900	6.1
Chromium	Cr	2 8 13 1	3+, 6+	1875	7.19
Manganese	Mn	2 8 13 2	2+, 3+, 4+, 7+	1245	7.43
Iron	Fe	2 8 14 2	2+, 3+	1536	7.86
Cobalt	Co	2 8 15 2	2+, 3+	1495	8.9
Nickel	Ni	2 8 16 2	2+	1453	8.9
Copper	Cu	2 8 18 1	1+, 2+	1083	8.96
Zinc	Zn	2 8 18 2	2+	420	7.14
Molybdenum	Mo	2 8 18 13 1	2+, 3+, 4+, 5+, 6+	2610	10.2
Silver	Ag	2 8 18 18 1	1+	961	10.5
Cadmium	Cd	2 8 18 18 2	2+	321	8.65
Tungsten (wolfram)	W	2 8 18 32 12 2	2+, 3+, 4+, 5+, 6+	3410	19.3
Gold	Au	2 8 18 32 18 1	1+, 3+	1063	19.3
Mercury	Hg	2 8 18 32 18 2	1+, 2+	−38	13.6

Cobalt is a component of vitamin B_{12}. Deficiency leads to pernicious anemia. Vitamin B_{12} is found only in meat and meat products. One hazard of a strict vegetarian diet is vitamin B_{12} deficiency.

Iron, cobalt, copper, zinc, manganese, and molybdenum are essential to the proper functioning of certain enzymes. These metallo-enzymes are necessary to life, but the exact function of the metal ion is not always known.

Problems

1. Define each term.
   a. inorganic chemistry
   b. organic chemistry
   c. noble gas
   d. halogen
   e. alkali metal
   f. alkaline earth metal
2. Give the electron dot symbol for each of these elements.
   a. neon
   b. oxygen
   c. fluorine
   d. potassium
   e. barium
   f. nitrogen
3. What is the outstanding chemical property of the noble gases? What structural feature accounts for this property?
4. Why is helium preferred to hydrogen for filling dirigibles, even though the latter has greater lifting power? What advantage does helium have over nitrogen in breathing mixtures for deep-sea divers? For someone with emphysema?
5. What function does argon serve in an electric light bulb?
6. How does a neon sign work?
7. Give the electron dot symbol for each of the following.
   a. fluoride ion
   b. iodide ion
   c. oxide ion
   d. sulfide ion
   e. potassium ion
   f. strontium ion
8. List one use for each element or compound.
   a. chlorine
   b. iodine
   c. NaF
   d. AgBr
   e. NaI
   f. NH_3
   g. NH_4NO_3
   h. Li_2CO_3
   i. NaCl
9. What is the effect on tooth enamel of small amounts of fluoride? Of excess fluoride in the diet?
10. What are basic oxides? What are acidic oxides?
11. Complete and balance the following equations.
   a. $Li + O_2 \rightarrow$

b. $Ca + O_2 \rightarrow$
c. $S + O_2 \rightarrow$
d. $CaO + H_2O \rightarrow$
e. $SO_2 + H_2O \rightarrow$
f. $Ca + S \rightarrow$

12. What is photochemical smog? What chemical compound starts the formation of photochemical smog by absorbing sunlight?
13. What is synergism?
14. What are allotropes? Name two sets of allotropes.
15. How do oxygen atoms, oxygen molecules, and ozone differ in structure and properties?
16. Explain the difference, in terms of effects on health, of ozone in the upper atmosphere and at ground level.
17. How does the burning of sulfur-containing coal lead to acid rain?
18. Explain the terms *London smog*, *Los Angeles smog*, and *greenhouse effect*.
19. What is nitrogen fixation? Why is it important?
20. How can a petroleum shortage lead to a scarcity of fertilizer?
21. What condition(s) lead(s) to formation of carbon monoxide during combustion?
22. How does carbon monoxide exert its poisonous effect?
23. What two alkali metal ions play a major role in maintaining fluid balance in the body?
24. What is berylliosis?
25. What important molecule in plants incorporates magnesium?
26. Name two functions of calcium ions in the body.
27. What is hard water? How does it affect the action of soaps?
28. List three distinguishing characteristics of transition metals.
29. List four transition metals essential to life. Indicate their function in the body.

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chapter 14

Hydrocarbons

At the beginning of the previous chapter we described the historical origin of the division of chemistry into organic and inorganic areas. Scientists of the 18th and 19th centuries studied compounds isolated from rocks and ores, from the atmosphere and the oceans, and called these inorganic because they were derived from nonliving systems. Other compounds were obtained from plants and animals, including human beings, and were called organic, meaning isolated from organized (living) systems. As chemists began to make "organic" compounds in the laboratory and found how essential to life some inorganic compounds were, organic chemistry was redefined simply as the chemistry of the compounds of carbon. People who speak of organic shampoos, organic foods, and organic fertilizers seem to invest their products with some special quality. To the chemist, the term just indicates that these materials contain carbon.

Figure 14.1 "Is it organic?" (From an idea by Cindy Hill.)

It may seem strange that we continue to divide the study of chemistry into two branches, organic and inorganic, with one branch dealing with the chemistry of one element and the other treating the chemistry of the more than a hundred other elements. As we progress through the next several chapters, the reason for the continued division will become obvious. Over 3 million compounds have been characterized. The overwhelming majority, more than 90%, contain carbon. Theoretically, the number of carbon compounds is infinite. Indeed, for the simplest family of organic compounds, the hydrocarbons, an infinite variety can be imagined. To avoid being overwhelmed by sheer numbers, we shall approach our study of organic chemistry one family at a time, concentrating, at first, on the simpler members of each family. This study will eventually lead to a consideration of those molecules which do deserve to be called organic in the old sense of that word—complex, carbon-containing molecules that determine the form of living systems. Such molecules, of course, are of vital interest to the biologist as well as to the chemist.

14.1 The Unique Nature of Carbon Atoms

Why so many carbon compounds? We can offer at least three reasons. One is that carbon atoms can bond with themselves to form chains of indefinite length. Most other elements are quite limited in this regard. When more than two or three atoms of an element other than carbon become bonded to one another, the compound formed is unstable. Ozone (O_3), for example, has a tendency to break apart, with explosive force if it is present in high concentrations. The process of chain formation, called *catenation*, results in a large number of carbon compounds. The chains may be branched. They may even be joined in rings.

Another reason for the many carbon compounds is that carbon, located in the middle of the periodic chart, forms strong covalent bonds to other elements such as hydrogen, oxygen, nitrogen, sulfur, and the halogens. These *substituent* atoms (atoms attached to a chain of carbon atoms), alone or in combination, make possible a still greater variety of carbon-containing compounds.

The third reason for the vast array of carbon compounds is isomerism; carbon compounds with the same number and kind of atoms can have more than one structural arrangement. This phenomenon will be discussed more fully in section 14.3.

14.2 Organic vs. Inorganic: A Simplistic Approach

Organic compounds, like inorganic ones, obey all the natural laws. Indeed, there is often no clear distinction in chemical or physical properties between organic and inorganic molecules. Nevertheless, it may be useful to compare and contrast typical members of each class. Keep in mind, though, that there will be many exceptions to the generalizations made here. Indeed, one might find a particular inorganic compound that has precisely those properties that we give here for typical organic compounds, and vice versa. With that hazard well in mind, let us proceed.

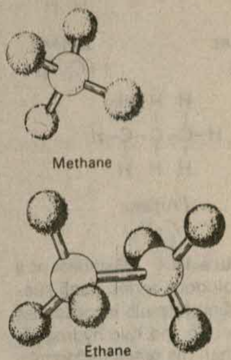
Most organic compounds have relatively low melting points; many exist as liquids at room temperature. For example, benzene (C_6H_6) boils at 80 °C and freezes at 5.5 °C. On the other hand, the only common inorganic compound which is a liquid at room temperature is water. The typical inorganic substance (e.g., sodium chloride) is a solid with a high melting point. Sodium chloride melts at 801 °C.

The typical organic compound is insoluble in water. Most are less dense than water and will float on top of water if we attempt to dissolve them. The typical inorganic compound is readily soluble in water.

The typical organic compound is highly flammable, a point that is important to remember when working in the laboratory. Examples are anesthetic ether, which forms explosive mixtures with air, and gasoline, a mixture of compounds used as fuel in internal combustion engines. Typical inorganic compounds are nonflammable. Indeed, inorganics such as water, baking soda (sodium bicarbonate, $NaHCO_3$), and borax ($Na_2B_4O_7 \cdot 10\ H_2O$) are used in fighting fires. Sodium bicarbonate is one of the few carbon-containing compounds classified with the inorganics.

These and other typical properties reflect the fact that most organic compounds are composed of molecules with covalent bonds. The typical inorganic compound is ionic. Don't forget, though, that there are covalent inorganic compounds (water, for example). And we will encounter a few ionic organics.

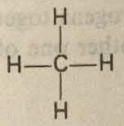
14.3 Alkanes: The Saturated Hydrocarbons


Methane

Ethane

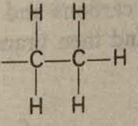
Figure 14.2 Ball-and-stick models of methane and ethane.

Before one can even begin to understand the large, complex molecules on which life is based, it is necessary to learn something about simpler molecules. We will start with organic compounds containing only two elements, carbon and hydrogen. These compounds are called hydrocarbons (a name which, you will have to admit, is reasonable). In sections 4.12 and 4.14, we encountered compounds called methane (CH_4) and ethane (C_2H_6). Models of molecules of these two compounds are shown in **figure 14.2.** These are the first two members of a series of related compounds called *alkanes* or *saturated hydrocarbons. Saturated*, in this case, means that each carbon atom is bonded to four other atoms; there are no double or triple bonds in the molecules. Structurally, methane and ethane are generally represented as



$$\begin{array}{ccccc} & & H & & \\ & & | & & \\ H & - & C & - & H \\ & & | & & \\ & & H & & \end{array}$$

Methane



$$\begin{array}{ccccccc} & & H & & H & & \\ & & | & & | & & \\ H & - & C & - & C & - & H \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

Ethane

These representations make no attempt to accurately portray bond angles in particular, or molecular geometry in general. You should keep the models in mind when you look at these flat pictures. (The bond angles and molecular geometry of methane were described in detail in section 4.12.)

Natural gas consists largely of methane, with some ethane and smaller amounts of other hydrocarbons containing three to five carbon atoms.

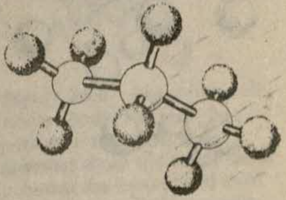
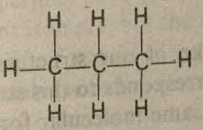


Figure 14.3 Ball-and-stick model of propane.

The three-carbon hydrocarbon (C_3H_8) is called propane. A ball-and-stick model of this compound is shown in **figure 14.3.** In two dimensions, the structure is generally written



$$\begin{array}{ccccccccc} & & H & & H & & H & & \\ & & | & & | & & | & & \\ H & - & C & - & C & - & C & - & H \\ & & | & & | & & | & & \\ & & H & & H & & H & & \end{array}$$

Propane

Notice that methane, ethane, and propane form a series in which the adjacent members differ by one carbon atom and two hydrogen atoms, that is, by a CH_2 unit (**figure 14.4**). Compounds related in this way are said to make up a *homologous series*. Such a series has properties which vary in a regular and predictable manner. The principle called *homology* gives meaning to organic chemistry in much the same way that the periodic table gives

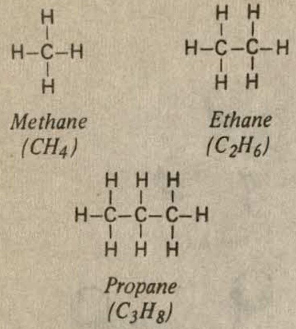


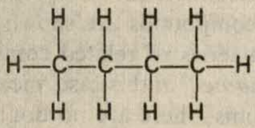
Figure 14.4 Members of a homologous series. Each succeeding formula incorporates one carbon and two hydrogens more than the previous formula.

organization and meaning to the chemistry of the elements. Instead of a bewildering array of individual carbon compounds, we can study a few members of a homologous series (called homologs), and from them we can deduce the properties of other compounds in the series.

Continuing the homologous series, we add another carbon atom and a pair of hydrogens to get C_4H_{10}. It is rather easy to write a structure corresponding to this formula. We merely string 4 carbon atoms in a row,

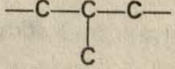
—C—C—C—C—

and then we add enough hydrogen atoms to give each carbon atom four bonds.



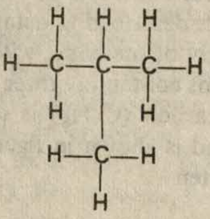
$$H-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-H$$

There is a compound called butane which has this structure. But there is another way to put 4 carbons and 10 hydrogens together. String out 3 of the 4 carbon atoms, and then branch the other one off the middle carbon of the chain.



$$-C-\underset{C}{C}-C-$$

Now we add enough hydrogen atoms to give each carbon four bonds.



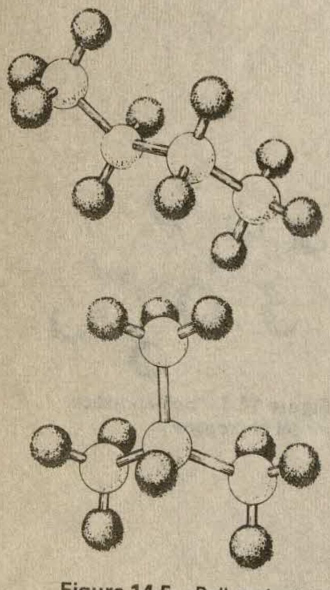
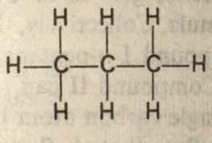
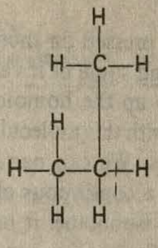


Figure 14.5 Ball-and-stick models of *n*-butane and isobutane.

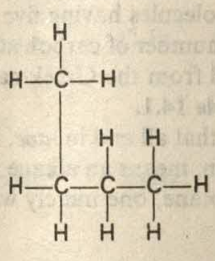
And, fortunately for the sake of our structural theory, there is another gaseous hydrocarbon that corresponds to this structure. There are two compounds, then, that have the same molecular formula, C_4H_{10}. One boils at 0 °C; the other, at −12 °C. Different compounds with the same molecular formula are called *isomers*. To give the two butanes unique names, we call the one with the continuous chain of carbon atoms normal butane, or *n*-butane. The one with the branched chain is called isobutane. **Figure 14.5** shows ball-and-stick models of the two isomeric butanes.

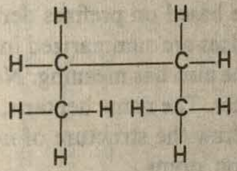
The three smaller homologs of this series do not exist as isomers. There is only one methane, one ethane, and one propane. We could draw what might appear to be different propanes.

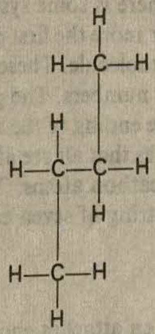




But these drawings just demonstrate the limitations of flat pictures. If we made a ball-and-stick model of propane, the one model could be made to resemble both of the flat structural formulas. We could also offer several alternate drawings of the *n*-butane formula.







As in the case of propane, the variety of drawings of *n*-butane represents the same compound. All the structural formulas show a continuous four-carbon chain. This chain may be twisted or bent, but it is still one continuous chain. The different arrangements for the four-carbon chain result from the fact that the various parts of the molecule are free to spin about the single bonds which join them to the rest of the molecule. Look at **figure 14.6**, and focus your attention on the bond between the second and third carbon atoms in the chain. We are spinning the right end of the molecule about this bond. You can see that the relative position of the carbon atom on the right end changes. Spinning can take place about any of the bonds in this compound, and that is what permits us to draw seemingly distinct formulas. The formulas do not represent isomers, but the same compound. Isobutane is a true isomer of *n*-butane. The formula of isobutane shows a continuous chain of three carbon atoms only, with the fourth carbon atom attached as a branch off the middle carbon of the continuous chain. If **figures 14.5** and **14.6** do not make this point clear, you should make models to convince yourself. (Borrow ball-and-stick models or create some of your own from marshmallows and toothpicks.)

Propane and the butanes are familiar fuels. They are usually supplied under pressure in tanks. Although they are gases at ordinary temperatures and under normal atmospheric pressure, they are liquefied under pressure and are sold as liquefied petroleum (LP) gas. Butane, liquefied under pressure, can be seen in the popular disposable butane cigarette lighters. When

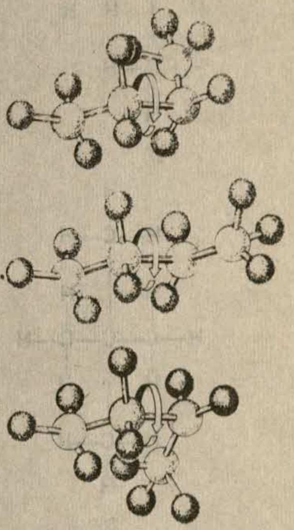
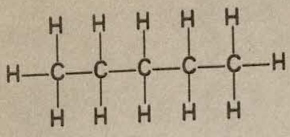
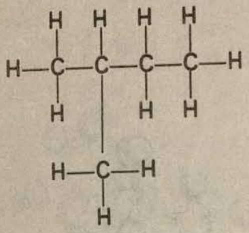


Figure 14.6 Rotation about single bonds. The right-hand portion of the molecule is spinning about the single bond between the second and third carbon atoms. The *same* molecule can thus assume different arrangements.



$$H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$$

I



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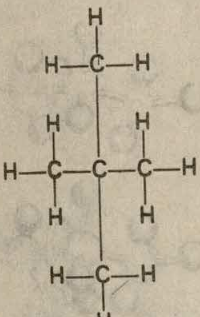


III

the release lever is pressed on these lighters, the butane comes under atmospheric pressure, and some of it vaporizes and is ignited by a spark.

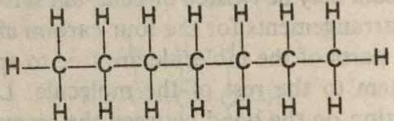
One more step up the homologous series gets us to C_5H_{12}. There are three compounds with this molecular formula. Collectively, these compounds are called pentanes. We can name compound I *n*-pentane, because it has all five carbons in a continuous chain. Compound II can be called isopentane, because, like isobutane, it has a single carbon atom branched off the second carbon of the continuous chain. But what shall we call compound III? Let's name it the way the chemists did when it was discovered in 1870. Since the other two pentanes were characterized first, this one was called neopentane (from the Greek *neos,* "new").

As incredibly complex as hydrocarbon chemistry may appear to you by now, there is some system to it. For example, for molecules having five carbons or more the first part of the name indicates the number of carbon atoms in the molecule. These are based on prefixes derived from the Greek names for the numbers. The prefixes are summarized in **table 14.1.**

The ending of the name also has meaning. Note that all end in *-ane*. This indicates that all are alkanes. The name **heptane**, then, means an alkane with seven carbon atoms. To draw the structure of *n*-heptane, one merely writes out a string of seven carbon atoms,

—C—C—C—C—C—C—C—

and then attaches enough hydrogens to give each carbon a valence of four. This requires three hydrogens on each end carbon and two on each of the others.



$$H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$$

In this manner we can readily extend our list of structures of *normal* hydrocarbons to decane. These continuous-chain alkanes are shown in **table 14.2.** Notice that each molecular formula in that table differs from the one preceding it by a CH_2 unit, illustrating the principle of homology. Notice also that the number of isomers increases rapidly with increasing carbon

Table 14.1
Greek prefixes

Prefix	*Number*
Pent-	5
Hex-	6
Hept-	7
Oct-	8
Non-	9
Dec-	10

Table 14.2
The first 10 normal alkanes

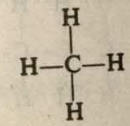
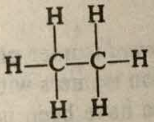
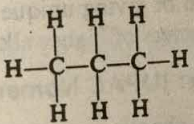
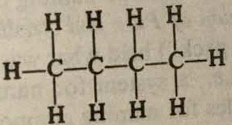
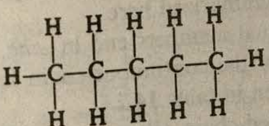
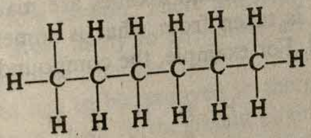
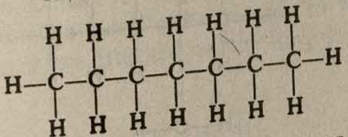
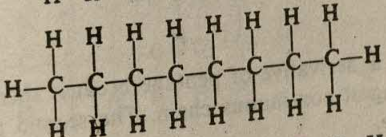
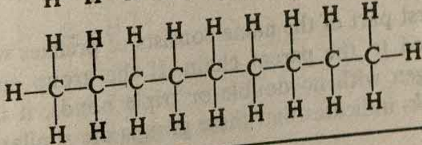
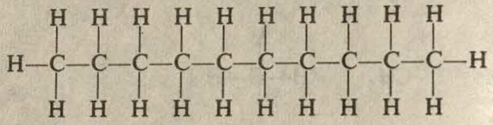
Name	*Molecular Formula*	*Structural Formula*	*Number of Possible Isomers*
Methane	CH_4	 $H-\underset{H}{\overset{H}{C}}-H$	1
Ethane	C_2H_6	 $H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$	1
Propane	C_3H_8	 $H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$	1
Butane	C_4H_{10}	 $H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$	2
Pentane	C_5H_{12}	 $H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$	3
Hexane	C_6H_{14}	 $H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$	5
Heptane	C_7H_{16}	 $H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$	9
Octane	C_8H_{18}	 $H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$	18
Nonane	C_9H_{20}	 $H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-H$	35

Table 14.2 (continued)

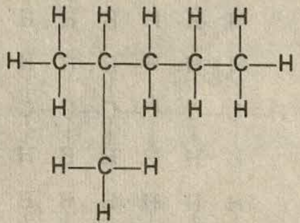
Name	*Molecular Formula*	*Structural Formula*	*Number of Possible Isomers*
Decane	$C_{10}H_{22}$	 $\mathrm{H-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-H}$	75

number. There are 5 hexanes (the *normal* isomer plus 4 others), 9 heptanes, and 18 octanes. There are over 4 billion isomers with the molecular formula $C_{30}H_{62}$. Fortunately, not all of those have been isolated or characterized. We've already run into a problem of giving unique names to the 5 hexanes, let alone the large numbers of isomers of higher alkanes.

14.4 The Universal Language: IUPAC Nomenclature

In order to bring order to the chaotic naming of newly discovered compounds, the *International Union of Pure and Applied Chemistry* (IUPAC—sometimes pronounced "you pack") held what was to be the first of several meetings on nomenclature (i.e., a system for naming) in 1892. This conference established formal rules for naming compounds. Some of the rules for naming alkanes are summarized here.

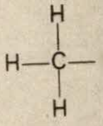
1. The names of individual members end in *-ane*, indicating that they are alkanes. The names of the continuous-chain members having up to 10 carbon atoms are given in **table 14.2.**
2. The names of branched-chain alkanes are made up of two parts. The end of the name is taken from what is sometimes referred to as the parent compound. For example, the compound



would be a derivative of pentane because there are five carbon atoms in the longest continuous chain. The second part of the name would be *pentane*.

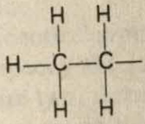
3. The first part of the name consists of prefixes which indicate the groups attached to the parent chain. If the group contains only carbon and hydrogen with no double or triple bonds, it is called an *alkyl* group. The *alk-* indicates that these groups are similar to alkanes; the *-yl* indi-

cates that a group of atoms are attached to some parent chain. Specific alkyl groups are named after the alkane with the same number of carbons. For example, the group



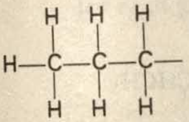
(or $CH_3—$)

is derived from methane and is called *methyl*. The alkyl group derived from ethane is

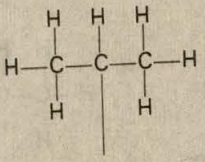


(or $CH_3CH_2—$)

It is called an *ethyl* group. Two alkyl groups can be derived from propane.



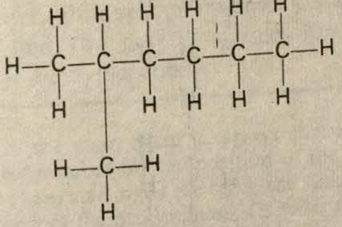
(or $CH_3CH_2CH_2—$)



(or $CH_3\underset{|}{C}HCH_3$)

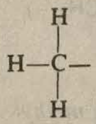
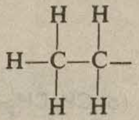
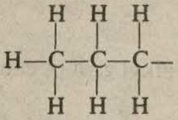
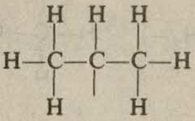
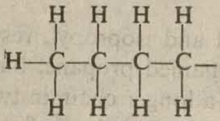
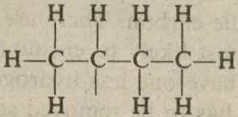
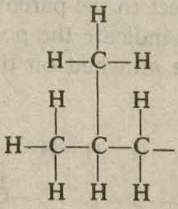
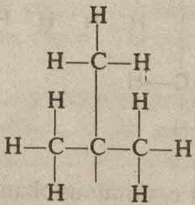
These are called *n*-propyl and isopropyl, respectively. Remember that there is only one alkane named propane, but a chain of three carbon atoms can be attached to a longer chain in two different ways. One has the attachment through an end carbon of the three-carbon chain; the other, through the middle carbon. There are many other alkyl groups. The ones that we are most likely to encounter are listed in **table 14.3.** Notice that the groups have one less hydrogen than the corresponding alkanes. This hydrogen has to be removed so there will be a free bond at which the group can connect to the parent chain.

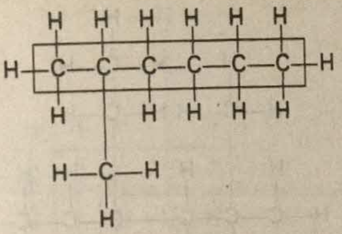
4. Arabic numerals are used to indicate the position to which the substituents (the alkyl groups) are attached on the longest chain. Thus, to name the compound



we first identify the longest continuous chain.

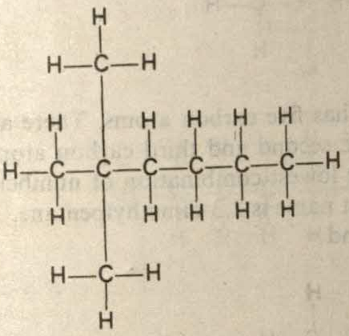
Table 14.3
Common alkyl groups

Name	Structural Formula	Condensed Structural Formula
Methyl		CH_3-
Ethyl		CH_3CH_2-
Derived from propane:		
Propyl (*n*-propyl)		$CH_3CH_2CH_2-$
Isopropyl		$CH_3\underset{\vert}{C}HCH_3$
Derived from *n*-butane:		
Butyl (*n*-butyl)		$CH_3CH_2CH_2CH_2-$
Secondary butyl (*sec*-butyl)		$CH_3\underset{\vert}{C}HCH_2CH_3$
Derived from isobutane:		
Isobutyl		$CH_3\overset{CH_3}{\overset{\vert}{C}}HCH_2-$
Tertiary butyl (*tert*-butyl)		$CH_3-\underset{\vert}{\overset{CH_3}{\overset{\vert}{C}}}-CH_3$

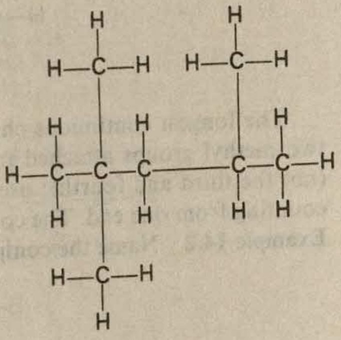


There are six carbon atoms in this chain. The compound is therefore a derivative of hexane. The group attached to the chain (CH_3—) is methyl. It is on the second carbon atom from the left end. Thus, the compound is 2-methylhexane.*

5. If two or more identical groups are attached to the main chain, a number is required to specify the location of each. Further, we must indicate whether there are two, three, or four identical groups hanging from the parent chain, and we do this by using the prefix *di-* for two, the prefix *tri-* for three, and the prefix *tetra-* for four. And even if two identical groups are located at the same position, the number must be repeated for each group.



2,2-Dimethylhexane

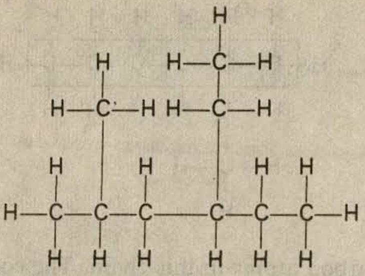


2,2,4-Trimethylpentane

(Notice from these examples that commas are used to separate numbers from each other and that hyphens are used to separate numbers from words.)

The official IUPAC rules state that the groups should be listed in alphabetical order, although many chemists still list them in order of increasing size and you may sometimes hear 4-ethyl-2-methylhexane called "2-methyl-4-ethylhexane."

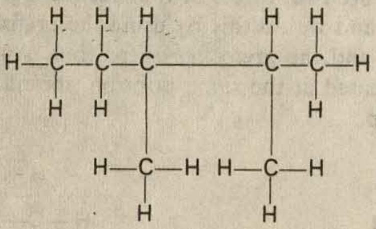
*The numbering of the main chain is always started at the end which will provide the lowest number for the position of the substituent. If we numbered the parent chain starting at the right, the substituent would be located at carbon number 5 of the parent chain. In order to obtain the lowest possible number for the substituent, then, we must count from left to right in this instance.



4-Ethyl-2-methylhexane

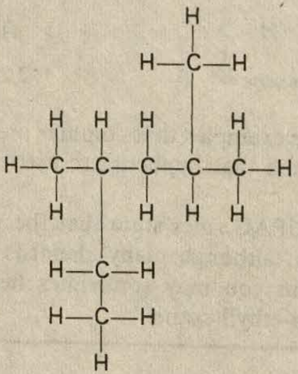
The best way to learn how to name alkanes is by working out examples, not just by memorizing rules. It's easier than it sounds. Try the following.

Example 14.1 Name the compound

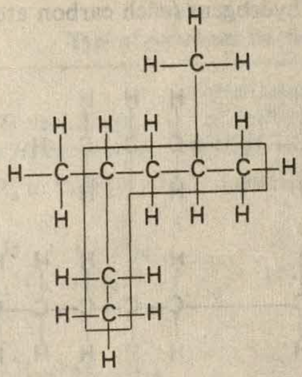


The longest continuous chain has five carbon atoms. There are two methyl groups attached to the second and third carbon atoms (not the third and fourth); use the lowest combination of numbers, counting from one end. The correct name is 2,3-dimethylpentane.

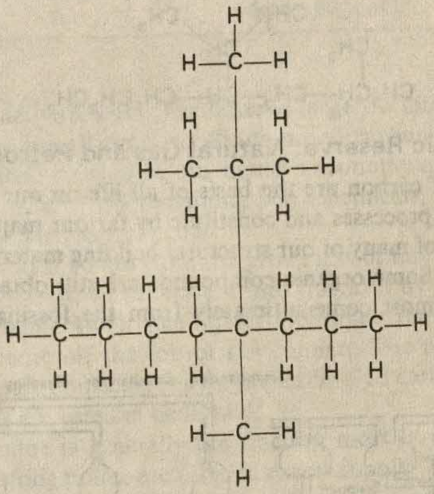
Example 14.2 Name the compound



The correct name is 2,4-dimethylhexane, not 2-ethyl-4-methylpentane. This is a fooler. The parent compound is the longest continuous chain, not necessarily the chain drawn straight across the page. In this compound, the longest chain contains six, not five, carbon atoms.



Example 14.3 Name the compound



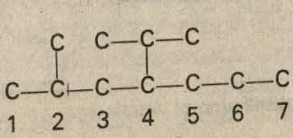
The correct name is 4-*tert*-butyl-4-methyloctane.

Example 14.4 Draw 2-methyl-4-isopropylheptane.

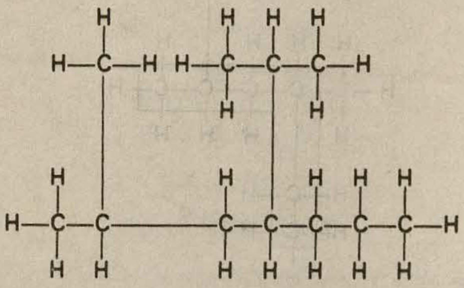
In drawing compounds, always start with the parent chain, heptane in this case.

—C—C—C—C—C—C—C—

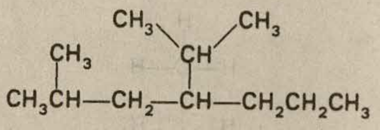
Then add the groups at their proper positions. You can number the parent chain from either direction as long as you are consistent (don't change directions in the middle of a problem).



Finally, fill in all the hydrogens (each carbon atom must have four bonds).



You can condense this formula by writing the hydrogens right next to the carbons to which they are attached.



$$\begin{matrix} & & CH_3\diagdown\ \diagup CH_3 & \\ CH_3 & & CH & \\ | & & | & \\ CH_3CH & —CH_2— & CH & —CH_2CH_2CH_3 \end{matrix}$$

14.5 Our Organic Reserve: Natural Gas and Petroleum

Compounds of carbon are the basis of all life on our planet. They are essential to all life processes and constitute by far our major energy source. They are the basis of many of our structural building materials and of nearly all our medicines. Some organic compounds are still obtained from plants and animals, but most come ultimately from the fossilized carbon com-

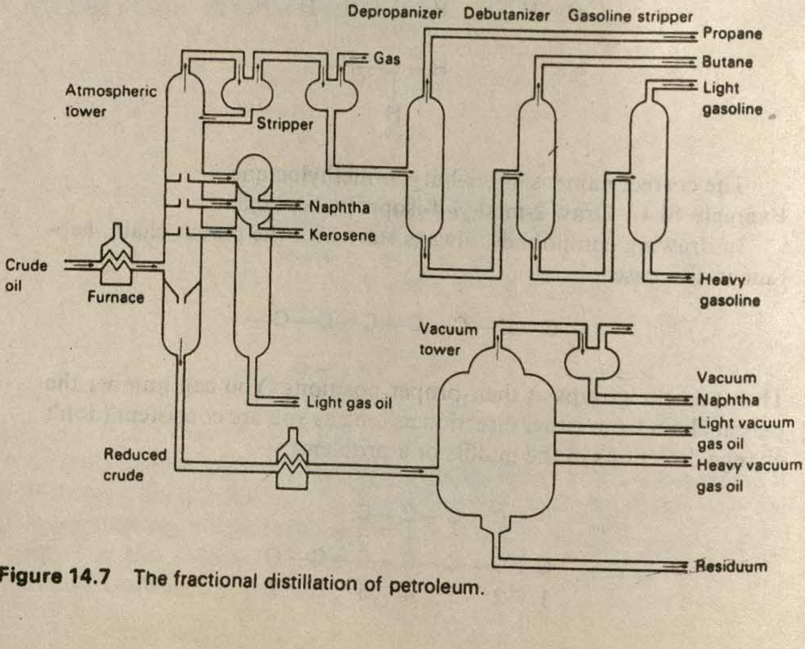


Figure 14.7 The fractional distillation of petroleum.

Table 14.4
Typical petroleum fractions

Fraction	*Typical Range of Hydrocarbons*	*Approximate Range of Boiling Point (in degrees Celsius)*	*Typical Uses*
Natural gas	CH_4 to C_4H_{10}	Less than 40	Fuel, starting materials for plastics
Gasoline	C_5H_{12} to $C_{12}H_{26}$	40–200	Fuel, solvents
Kerosene	$C_{12}H_{26}$ to $C_{16}H_{34}$	175–275	Diesel fuel, jet fuel, home heating; cracking to gasoline
Heating oil	$C_{15}H_{32}$ to $C_{18}H_{38}$	250–400	Industrial heating, cracking to gasoline
Lubricating oil	$C_{17}H_{36}$ and up	Above 300	Lubricants
Residue	$C_{20}H_{42}$ and up	Above 350 (some decomposition)	Paraffin, asphalt

pounds coal and petroleum. The latter is largely a mixture of alkanes, with the molecules having from 1 to 40 (or more) carbon atoms each. Most of the *petrochemicals* so vital to our modern economy are derived from these alkanes. A portion of the remaining petrochemicals, called *aromatics* (section 14.15), are derived from coal.

Petroleum, as it comes from the ground, is of limited use. So that it will better suit our needs, we separate it into fractions by boiling it in a distillation column (**figure 14.7**). The lighter molecules, those with 1 to 4 carbon atoms each, come off the top of the column. The next fraction contains, for the most part, molecules having from 5 to 12 carbon atoms. These and other fractions are listed in **table 14.4.**

Since gasoline is generally the fraction most in demand, the fractions with higher boiling points are often in excess supply. These can be converted to gasoline by heating in the absence of air. This process, called *cracking,* breaks the big molecules apart. The process is illustrated in **figure 14.8,** where $C_{14}H_{30}$ is used as an example. Not only does cracking convert some of the molecules into those in the gasoline range (those having from 5 to 12 carbon atoms), but it results in a variety of useful by-products. The *unsaturated hydrocarbons* (section 14.9) are starting materials for the manufacture of many plastics, detergents, and drugs—indeed a whole host of petrochemicals. Present and future shortages of petroleum will mean a great deal more than just scarce, high-priced gasoline.

The cracking process described here is a crude, yet illustrative, example of how chemists modify nature's materials to meet our needs and desires. Starting with coal tar or petroleum, the chemist can create a dazzling array of substances with a wide variety of properties. These include plastics, pain killers, antibiotics, stimulants, depressants, and detergents, to name just a few. Many of these materials will be discussed in subsequent chapters. Before going on, though, let's look at gasoline in more detail.

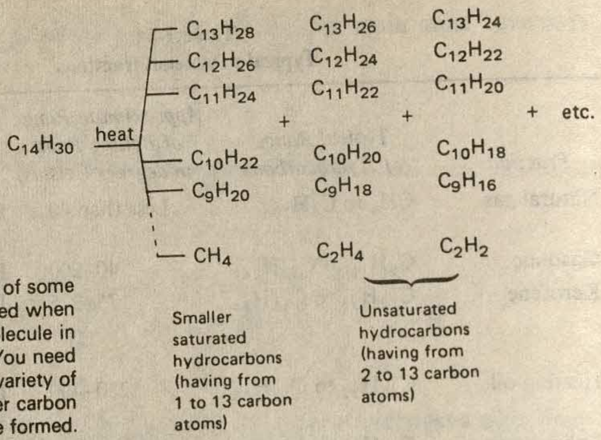
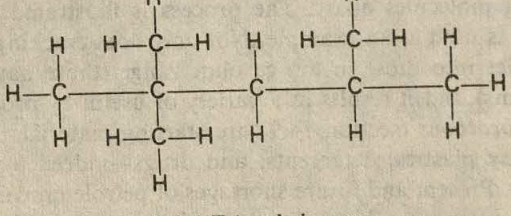


Figure 14.8 Formulas of some of the products formed when $C_{14}H_{30}$ (a typical molecule in gasoline) is cracked. You need only note that a great variety of hydrocarbons with fewer carbon atoms are formed.

We have already indicated that gasoline is largely a mixture of hydrocarbons with formulas ranging from C_5H_{12} up to $C_{12}H_{26}$. Since there are many, many isomeric forms (particularly for the hydrocarbons with many carbon atoms), we see that gasoline is an exceedingly complex mixture of alkanes. In addition to the alkanes, there are also small amounts of other kinds of hydrocarbons (some of them described in the following paragraphs) and even some sulfur- and nitrogen-containing compounds present in the gasoline fraction of petroleum. Other compounds that improve the fuel in a variety of ways are intentionally added, as we shall see.

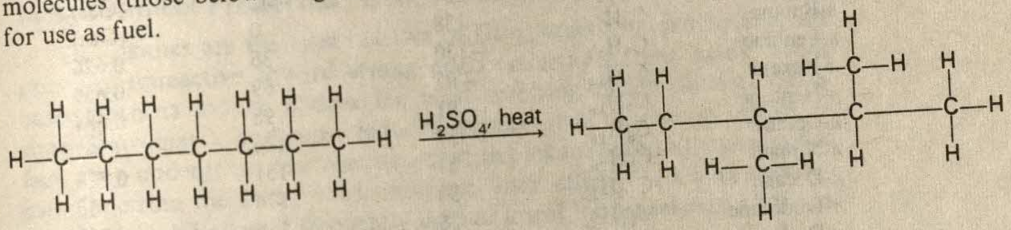
Early in the development of the automobile engine, scientists learned that some types of hydrocarbons burned more evenly and were less likely to ignite prematurely than others. Ignition before the piston was in proper position led to a "knocking" in the engine. Scientists were soon able to correlate good performance with a branched-chain structure in hydrocarbon molecules. An arbitrary performance standard was established in 1927. The best performer in the laboratory test engine was found to be a compound incorrectly called "isooctane."



2,2,4-Trimethylpentane
("isooctane")

This compound, properly named 2,2,4-trimethylpentane, was assigned a value of 100 "octane." An unbranched-chain compound, *n*-heptane, was found to cause a very bad knock. It was given an octane rating of 0. A gasoline rated 90 octane is one which performs the same as a mixture which is 90% "isooctane" and 10% *n*-heptane.

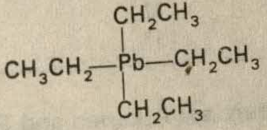
In the 1930s chemists discovered that they could improve the octane rating of gasoline by heating it in the presence of certain catalysts such as sulfuric acid (H_2SO_4) and aluminum chloride ($AlCl_3$). This increase in octane rating was attributed to conversion (isomerization) of some of the unbranched molecules in the gasoline mixture to highly branched molecules. For example, *n*-heptane molecules might be "isomerized" to a branched structure. Chemists were also able to combine small hydrocarbon molecules (those below the gasoline range) into larger, more suitable ones for use as fuel.



n-*Heptane*

2,3-Dimethylpentane

They also discovered certain chemical substances which, when added in small amounts, substantially improved the antiknock quality of gasoline. Chief among these *additives* was tetraethyl lead.



$$CH_3CH_2-\overset{\displaystyle CH_2CH_3}{\underset{\displaystyle CH_2CH_3}{Pb}}-CH_2CH_3$$

This compound, when added in amounts as small as 1 ml per litre of gasoline (about 0.1 fl oz per gallon, or 1 part per thousand), would increase the octane rating from approximately 55 to 90 or more. The addition of this lead compound has come under attack in recent years. Not only is lead toxic to people and other living things, but it also fouls the catalytic converters placed on automobiles to reduce the concentration of certain air pollutants.

14.6 Physical Properties of the Alkanes

The alkanes form a homologous series. The properties of the members vary in a regular and predictable manner. For example, their boiling points show a fairly regular increase of from 20 to 30 °C as we go up the series (**table 14.5**).

You should note from the table that at room temperature alkanes having from 1 to 4 carbon atoms per molecule are gases, the normal alkanes having from 5 to about 16 carbon atoms per molecule are liquids, and alkanes having more than 16 carbon atoms per molecule are solids. Note also that the densities of the liquid alkanes are less than that of water (1.0 g/ml). The alkanes are essentially insoluble in water and hence will float on top of water. Alkanes dissolve many organic substances of low polarity, such as fats, oils, and waxes. Mixtures of alkanes are therefore frequently used as organic solvents.

Table 14.5
Physical properties of selected alkanes

Name	*Molecular Formula*	*Melting Point (in degrees Celsius)*	*Boiling Point (in degrees Celsius)*	*Density at 20 °C (in grams per millilitre)*
Methane	CH_4	−183	−162	(Gas)
Ethane	C_2H_6	−172	−89	(Gas)
Propane	C_3H_8	−187	−42	(Gas)
n-Butane	C_4H_{10}	−138	0	(Gas)
n-Pentane	C_5H_{12}	−130	36	0.626
n-Hexane	C_6H_{14}	−95	69	0.659
n-Heptane	C_7H_{16}	−91	98	0.684
n-Octane	C_8H_{18}	−57	126	0.703
n-Nonane	C_9H_{20}	−54	151	0.718
n-Decane	$C_{10}H_{22}$	−30	174	0.730
n-Undecane	$C_{11}H_{24}$	−26	196	0.740
n-Dodecane	$C_{12}H_{26}$	−10	216	0.749
n-Tridecane	$C_{13}H_{28}$	−6	235	0.757
n-Tetradecane	$C_{14}H_{30}$	6	254	0.763
n-Pentadecane	$C_{15}H_{32}$	10	271	0.769
n-Hexadecane	$C_{16}H_{34}$	18	280	0.775
n-Heptadecane	$C_{17}H_{36}$	22	302	(Solid)
n-Octadecane	$C_{18}H_{38}$	28	316	(Solid)
n-Nonadecane	$C_{19}H_{40}$	32	330	(Solid)
n-Eicosane	$C_{20}H_{42}$	37	343	(Solid)

14.7 Physiological Properties: Alkanes and People

The physiological properties of alkanes vary in a regular way as we proceed through the homologous series. Methane appears to be totally physiologically inert. We could breathe a mixture of 80% methane and 20% oxygen without ill effect. Such a mixture would be flammable, however, and no fire or spark of any kind could be permitted in an atmosphere consisting of methane. Breathing an atmosphere of pure methane (the "gas" of a gas-operated stove) can lead to death not so much because of the presence of methane but because of the absence of oxygen (asphyxia). The other gaseous alkanes (and vapors of volatile liquid ones) act as anesthetics in high concentrations. They can also produce asphyxiation by excluding oxygen.

Liquid alkanes have varied effects depending on the part of the body exposed. On the skin, alkanes dissolve body oils. Repeated contact may cause dermatitis. Swallowed, alkanes do little harm while in the stomach. However, in the lungs, alkanes cause "chemical pneumonia" by dissolving fatlike molecules from the cell membranes in the alveoli. The cells become less flexible, and the alveoli are no longer able to expel fluids. The buildup of fluids is similar to that which occurs in bacterial or viral pneumonia. People who swallow gasoline, petroleum distillates, or other liquid alkane mixtures should not be made to vomit. That would increase the chance of their getting the alkane into the lungs.

Heavier liquid alkanes, when applied to the skin, act as emollients (skin softeners). Such alkane mixtures as mineral oil can be used to replace natural skin oils washed away by frequent bathing or swimming. Petroleum jelly (*Vaseline* is one brand) is a semisolid mixture of hydrocarbons which can be applied as an emollient or simply as a protective film. Water and water solutions (e.g., urine) will not dissolve such a film, which explains why petroleum jelly protects a baby's tender skin from diaper rash.

14.8 Chemical Properties: Little Affinity

The alkanes are the least reactive of all organic compounds. They are generally unreactive toward strong acids (such as sulfuric acid), strong bases (such as sodium hydroxide), most oxidizing agents (such as potassium dichromate), and most reducing agents (such as sodium metal). In fact, they undergo so few reactions that the alkanes are sometimes called *paraffins,* from the Latin words meaning "little affinity." Paraffin wax is a mixture of solid alkanes frequently used as a seal for homemade preserves. The inertness of the wax makes it ideal for such use.

The alkanes do undergo a few important reactions. When mixed with oxygen at room temperature, alkanes give no apparent reaction. However, when a match flame or spark supplies sufficient energy to get things started (the energy of activation), an exothermic (heat-producing) reaction proceeds vigorously. The reaction, which is called *combustion,* is illustrated for methane.

$$CH_4 + 2\,O_2 \longrightarrow CO_2 + 2\,H_2O + \text{heat}$$

If the reactants are adequately mixed and there is sufficient oxygen, the products are carbon dioxide, water, and the all-important heat (for cooking foods, heating homes, and drying clothes). Such ideal conditions are rarely met, however, and other products than carbon dioxide, water, and heat are frequently formed. When the oxygen supply is limited, carbon monoxide is a by-product. At the high temperatures achieved in some combustion reactions, some nitrogen (which, you will recall, makes up 80% of the atmosphere in which the fuel is burned) is converted to oxides. Further, petroleum usually contains some sulfur compounds, and combustion reactions involving sulfur will yield sulfur dioxide. Thus, the same combustion reactions that heat our homes, power our industries, and propel our automobiles also produce most of our air pollution.

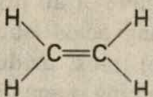
In addition to undergoing combustion, alkanes react with fluorine, chlorine, and bromine. Such reactions produce halogenated hydrocarbons. These important compounds will be discussed in the next chapter.

Alkanes can also be converted to protein. Certain varieties of yeasts, when mixed with oil and supplied with the proper minerals, are able to convert hydrocarbons to proteins. To date, problems of oily taste and residual toxicity have prevented proteins derived from petroleum from being an important source of food for humans. Besides, we have a shortage of petroleum for fuels and petrochemicals. It isn't likely that we will divert a substantial portion to be converted into proteins.

14.9 Alkenes: Structure and Nomenclature

Not all hydrocarbons are as resistant to reaction as the alkanes. In fact, the next family that we will consider is quite reactive. This family, called *alkenes* (note the *-ene* ending), is characterized by the presence of a carbon-to-carbon double bond. Names, structures, and physical properties of a few representative alkenes are given in **table 14.6.**

We have used only condensed structural formulas in this table. Such formulas are much easier to set in type, but they are sometimes confusing to newcomers to organic chemistry. Thus, $CH_2=CH_2$ stands for



The double bond is shared by the two carbon atoms and does not involve the hydrogens, although the condensed formula does not make this point obvious. **Figure 14.9** shows a ball-and-stick model of this compound, ethylene. For $CH_3(CH_2)_3CH=CH_2$ (1-hexene), the full structural formula would be

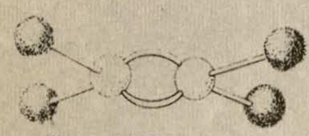
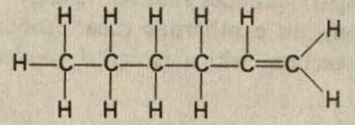


Figure 14.9 Ball-and-stick model of ethylene.



The $(CH_2)_3$ in the condensed formula means that three CH_2 units are connected in series to one another. The hydrogen written to the left of the double bond in the condensed formula is understood to be hanging off the carbon atom immediately preceding it.

Compare the molecular formulas of the alkenes in **table 14.6** to those for the alkanes in **table 14.2.** The molecular formula for ethane is C_2H_6. The formula for the two-carbon alkene is C_2H_4. Each alkene has two fewer hydrogens than the corresponding alkane. Compared to the carbon atoms in an alkane, each of two carbon atoms in the alkene must bond to one less hydrogen atom in order to form the double bond. Since these carbons are sharing two of their bonds with one atom (and thus bonding to fewer different atoms), the compounds are said to be *unsaturated.*

The first two alkenes of **table 14.6,** ethene and propene, are most often called by their common names, ethylene and propylene, respectively. Ethylene ($CH_2=CH_2$) is one of the most important of all commercial chemicals. In 1975, the United States chemical industry produced 9 000 000 000 kg (19 800 000 000 lb) of ethylene, making it the most important of all synthetic organic chemicals. Over one-third of this ethylene went into the manufacture of polyethylene, one of the most familiar plastics (chapter 21). Another one-sixth was converted to ethylene glycol, the major component of most brands of antifreeze for automobile radiators.

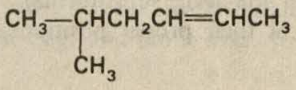
Propylene ($CH_3CH=CH_2$) is also an important industrial chemical. It is converted to plastics, isopropyl alcohol (chapter 16), and a variety of other end products and intermediates for synthesis.

Table 14.6
Physical properties of some selected alkenes

IUPAC Name	*Molecular Formula*	*Condensed Structure*	*Melting Point (in degrees Celsius)*	*Boiling Point (in degrees Celsius)*
Ethene	C_2H_4	$CH_2{=}CH_2$	−169	−104
Propene	C_3H_6	$CH_3CH{=}CH_2$	−185	−47
1-Butene	C_4H_8	$CH_3CH_2CH{=}CH_2$	−185	−6
1-Pentene	C_5H_{10}	$CH_3CH_2CH_2CH{=}CH_2$	−138	30
1-Hexene	C_6H_{12}	$CH_3(CH_2)_3CH{=}CH_2$	−140	63
1-Heptene	C_7H_{14}	$CH_3(CH_2)_4CH{=}CH_2$	−119	94
1-Octene	C_8H_{16}	$CH_3(CH_2)_5CH{=}CH_2$	−102	121

Before we consider the rest of the alkenes in **table 14.6,** let's pause to discuss the nomenclature of alkenes. While there is only one alkene with the formula C_2H_4 (ethene) and only one alkene with the formula C_3H_6 (propene), there are four alkenes with the formula C_4H_8. Common names are hardly helpful in naming the many isomers of the butenes and the higher alkenes. For the most part, the IUPAC system is used for these. Some of the IUPAC rules for alkenes are as follows.

1. All have names ending in *-ene*.
2. The longest chain of atoms *containing the double bond* is the parent compound. The name has the same stem as the corresponding alkane (i.e., the alkane with the same number of carbon atoms), but the ending is changed from *-ane* to *-ene*. Thus, the compound $CH_3CH{=}CH_2$, with three carbon atoms, is named *propene*.
3. When it is necessary to indicate the position of the double bond, the first carbon of the two which are doubly bonded is given the lowest possible number (i.e., the carbons are counted from the end of the chain nearer the first carbon of the double bond). For example, the compound $CH_3CH{=}CHCH_2CH_3$ has the double bond between the second and third carbon atoms. Its name is 2-pentene.
4. Substituent groups are named as usual. Their position is indicated by a number. Thus,

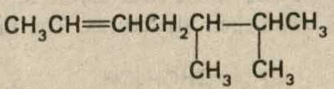


$$CH_3{-}\underset{\substack{|\\ CH_3}}{CH}CH_2CH{=}CHCH_3$$

is 5-methyl-2-hexene. Note that the numbering of the parent chain is always done in such a way as to give the double bond the lowest number, even if that forces a substituent to have a higher number. We say the double bond has priority in numbering.

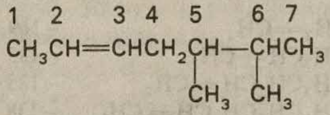
The rules are more easily learned through examples.

Example 14.5 Name the compound



$$CH_3CH{=}CHCH_2\underset{\substack{|\\ CH_3}}{CH}{-}\underset{\substack{|\\ CH_3}}{CH}CH_3$$

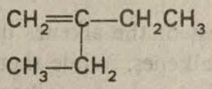
The longest continuous chain has seven carbon atoms. To give the first carbon of the double bond the lowest number, we start numbering from the left.



$$\overset{1}{C}H_3\overset{2}{C}H{=}\overset{3}{C}H\overset{4}{C}H_2\underset{\displaystyle CH_3}{\underset{|}{\overset{5}{C}}}H-\underset{\displaystyle CH_3}{\underset{|}{\overset{6}{C}}}H\overset{7}{C}H_3$$

The name of the compound is 5,6-dimethyl-2-heptene.

Example 14.6 Name the compound



$$CH_2{=}\underset{\displaystyle CH_3-CH_2}{\underset{|}{C}}-CH_2CH_3$$

The name is 2-ethyl-1-butene. The longest continuous chain in the molecule contains five carbon atoms. However, the longest continuous chain *containing the double bond* incorporates only four carbon atoms and this four-carbon chain serves as the parent compound.

Example 14.7 Draw 3,4-dimethyl-2-pentene.

To draw this compound, first write down the parent chain of five carbons.

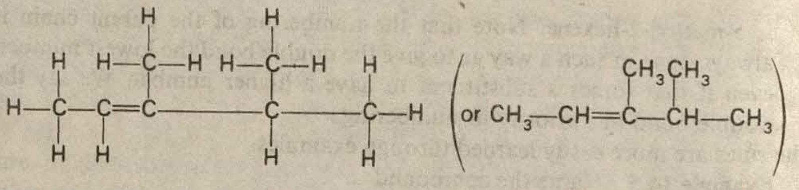
$$C—C—C—C—C$$

Then add the double bond between the second and third carbons (this is *2*-pentene).

$$\overset{1}{C}—\overset{2}{C}{=}\overset{3}{C}—\overset{4}{C}—\overset{5}{C}$$

You could have decided to count from right to left instead of from left to right. It doesn't matter as long as you are consistent (count the same way when you attach the substituents).

Now add the groups at their proper positions and fill in all the hydrogens.

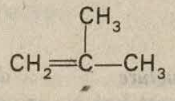


$$\left(\text{or } CH_3-CH{=}\overset{\displaystyle CH_3}{\overset{|}{C}}-\overset{\displaystyle CH_3}{\overset{|}{C}}H-CH_3\right)$$

Now back to **table 14.6** and those four isomeric butylenes (a common name for butenes). Let's write their structures. The first, 1-butene, is easy.

$$CH_2{=}CHCH_2CH_3$$

This structure corresponds to a gaseous compound which melts at −185 °C and boils at −6 °C. We can also draw a butylene analogous to isobutane.



$$CH_2{=}\overset{\displaystyle CH_3}{\overset{|}{C}}{-}CH_3$$

This compound is frequently called isobutylene, but its IUPAC name is methylpropene. Next we can write a structure for 2-butene.

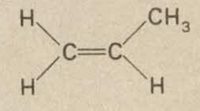
$$CH_3CH{=}CHCH_3$$

The carbon skeleton is the same as that of 1-butene, but the double bond is shared by the second and third carbon atoms instead of the first and second. The only problem is that there are *two* compounds that correspond to this formula for 2-butene. One melts at −139 °C and boils at +4 °C; the other melts at −106 °C and boils at +1 °C. The existence of two 2-butenes is explained by restricted rotation about the carbon-carbon double bond.

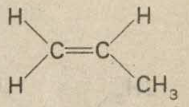
Remember that atoms and groups of atoms are free to spin about single bonds (section 14.3). However, two atoms connected by a double bond are not free to spin relative to one another. While the models in **figure 14.10** don't really "look" like the actual molecules (we can't see individual molecules), they do offer a mechanical equivalent of restricted rotation. The two connectors between the doubly bonded carbon atoms prevent these carbons from spinning as the singly bonded carbons are free to do. Thus, the two arrangements of 2-butene shown in **figure 14.10** really represent two different compounds. One cannot be converted to the other unless the double bond is broken first. To distinguish the two different isomers, one is called *cis*-2-butene and the other is *trans*-2-butene. The *cis* isomer is the one with both methyl groups on the same side of the double bond. In the *trans* isomer, the methyl groups are on opposite sides.

Table 14.7 summarizes the structures and some properties of the four isomeric butylenes.

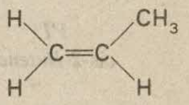
We can draw two *seemingly* different propylenes (structures IV and V). However, the second structure is not really different from the first. If you could pick it up from the page and flip it over, you would see that the two



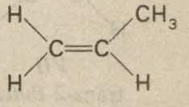
IV



V



IV



V

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Figure 14.10 Models of the 2-butenes. While the carbons joined by single bonds are free to spin about these bonds, the doubly bonded carbons are restricted in this regard.

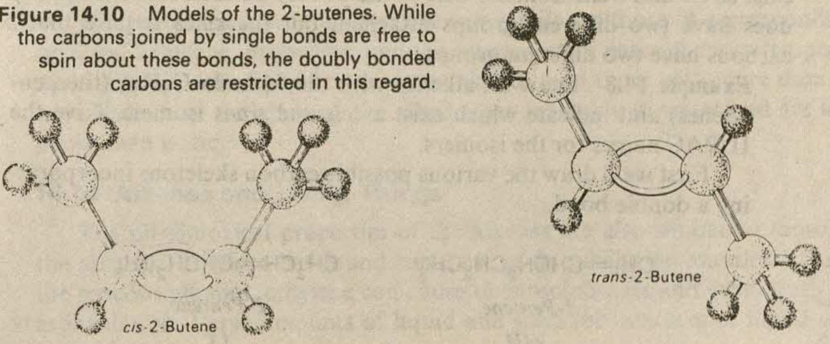
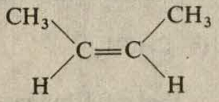
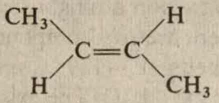
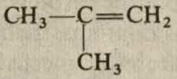
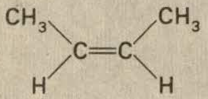
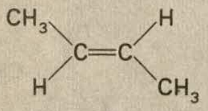


Table 14.7
Physical properties of the butylenes

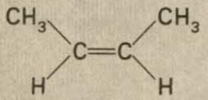
Name	*Structure*	*Melting Point (in degrees Celsius)*	*Boiling Point (in degrees Celsius)*
1-Butene	$CH_2{=}CHCH_2CH_3$	−185	−6
cis-2-Butene		−139	+4
trans-2-Butene		−106	+1
2-Methylpropene (isobutylene)	 $CH_3{-}\underset{\displaystyle CH_3}{\underset{\vert}{C}}{=}CH_2$	−140	−7



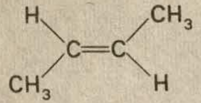
VI
cis-*2-Butene*



VII
trans-*2-Butene*



VI



VII
(flipped over)

formulas were identical. The same thing *cannot* be done with *cis* and *trans* isomers. If we start with these drawings of the two 2-butenes and then flip the *trans* isomer over, we see that the resulting structure is still clearly different from the *cis* isomer.

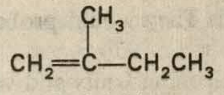
As the case of propylene proves, the mere presence of a double bond is not sufficient for *cis-trans,* or geometric, isomerism. The requirements for such isomerism are (1) that rotation be restricted in the molecule, *and* (2) that there be two nonidentical groups on *each* of the doubly bonded carbons. For 2-butene ($CH_3CH{=}CHCH_3$), the doubly bonded carbon on the left has a hydrogen group and a methyl group (two different groups), and the doubly bonded carbon on the right has a hydrogen group and a methyl group (two different groups). Thus, 2-butene exists as a *cis* and a *trans* isomer. Propene ($CH_3CH{=}CH_2$) has a doubly bonded carbon with two hydrogens (two identical groups) attached. The second requirement for geometric isomerism is not fulfilled, therefore, and this compound does *not* exist as *cis* and *trans* isomers. One of the doubly bonded carbons in propene does have two different groups attached, but the rules require that *both* carbons have two different groups.

Example 14.8 Draw all alkenes with the formula C_5H_{10} (the pentylenes) and indicate which exist as *cis* and *trans* isomers. Give the IUPAC names for the isomers.

First we'll draw the various possible carbon skeletons incorporating a double bond.

$CH_2{=}CHCH_2CH_2CH_3$
1-Pentene
VIII

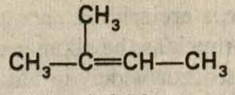
$CH_3CH{=}CHCH_2CH_3$
"2-Pentene"
IX



$CH_2{=}\overset{CH_3}{\overset{|}{C}}{-}CH_2CH_3$

2-Methyl-1-butene

X

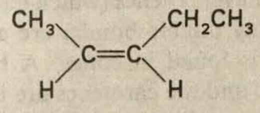


$CH_3{-}\overset{CH_3}{\overset{|}{C}}{=}CH{-}CH_3$

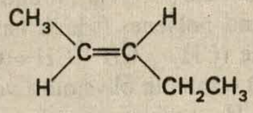
2-Methyl-2-butene

XI

Of these, only IX exists as *cis* and *trans* isomers.

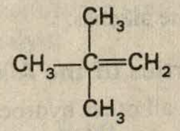


cis-*2-Pentene*



trans-*2-Pentene*

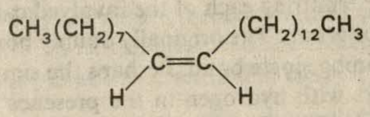
Structures VIII and X each have two hydrogens on one of their doubly bonded carbon atoms, and structure XI has two methyl groups on one of its doubly bonded carbons. Note that



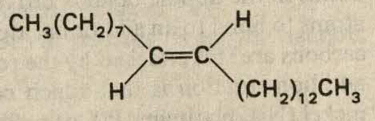
$CH_3{-}\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}{=}CH_2$

is not a possible isomer. The central carbon atom has five bonds in this structure, and carbon can form only four covalent bonds.

While geometric isomerism may seem of little practical importance to us, it is extremely important to houseflies. The female housefly secretes *cis*-9-tricosene as an attractant for the male. The latter has little, if any, affinity for the *trans* isomer.



cis-*9-Tricosene*



trans-*9-Tricosene*

Indeed, in most biological systems, the geometry of a molecule is of utmost importance.

Physical properties of alkenes are very similar to those of corresponding alkanes. Ethylene, propylene, and the butylenes are gases at room temperature. Alkenes with 5 to 18 carbons are liquids, and those with more than 18 are solids. Like the alkanes, the alkenes are insoluble in water and are less dense than water.

14.10 Alkenes and Living Things

The physiological properties of the alkenes are also similar to those of the alkanes. Ethylene has found some use as an inhalation anesthetic. Like the gaseous alkanes, ethylene can cause unconsciousness and even death by asphyxiation. Large amounts of liquid and solid (or mixtures of liquid and solid) alkenes are seldom encountered. They would probably act on or in our bodies much as the alkanes do.

Alkenes occur widely in nature. Ripening fruits and vegetables give off ethylene, which triggers further ripening. Food processors artificially introduce ethylene to hasten the normal ripening process; 1 kg of tomatoes can be ripened by exposure to as little as 0.1 mg of ethylene for 24 hours.

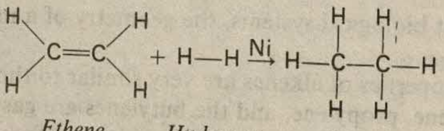
Other alkenes found in nature include 1-octene, found in lemon oil, and octadecene ($C_{18}H_{36}$), found in fish liver. Dienes (which have two double bonds) and polyenes (which have many double bonds) are also common. Butadiene ($CH_2{=}CH{-}CH{=}CH_2$) is found in coffee. A hexadecadiene ($C_{16}H_{30}$) occurs in olive oil. Lycopene and the carotenes are isomeric polyenes ($C_{40}H_{56}$) which give the attractive red, orange, and yellow colors to watermelons, tomatoes, carrots, and other vegetables and fruits. Vitamin A, essential to good vision, is derived from a carotene. Vitamin A is converted in the body to *trans*-retinene. The latter absorbs visible light and is converted to *cis*-retinene. It is this process, which occurs on the retina of the eye, that is responsible in part for vision. The world would be a much darker place without the chemistry of the alkenes.

14.11 Chemical Properties of the Alkenes

Like the alkanes—and all other hydrocarbons—the alkenes burn. While this is a hazard that you should remember when working with alkenes, these compounds are not commercially important as fuels. We can write an equation for the combustion of ethene which is similar to that for the combustion of an alkane.

$$C_2H_4 + 3\ O_2 \longrightarrow 2\ CO_2 + 2\ H_2O + \text{heat}$$

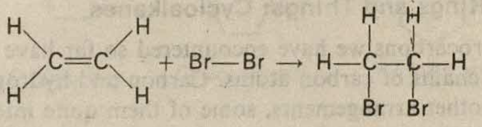
The typical reactions of the alkenes are *addition reactions*. One of the bonds in the double bond is broken, permitting each of the involved carbon atoms to bond to an additional atom or group. The originally doubly bonded carbons are still attached by the remaining single bond. Perhaps the simplest addition reaction is that which occurs with hydrogen in the presence of a nickel (Ni), platinum (Pt), or palladium (Pd) catalyst.



Ethene *Hydrogen* *Ethane*

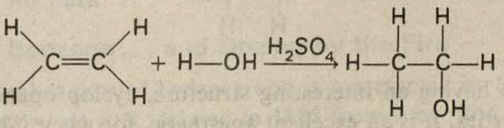
The product of this reaction is an alkane with the same carbon skeleton as the original alkene. *Hydrogenation* was once widely used in industry in the conversion of unsaturated vegetable oils into saturated fats. Hydrogenation of the liquid oil yields a solid fat and makes vegetable shortening resemble the more familiar animal fat, lard. The difference in the liquid oil and the solid fat is due to a difference in the number of double bonds present; there are more in the unsaturated oils and fewer in the saturated fats. Vegetable oils are now more readily accepted and, in fact, are frequently preferred by the consumer, but some oils are still hydrogenated so that the vegetable product will resemble an animal product. Margarine, for example, resembles butter by virtue of hydrogenation.

Alkenes readily add halogen molecules. Indeed, the reaction with bromine is often used to test for alkenes. Solutions of bromine are brownish red. When an alkene is added to such a solution, the color disappears because the alkene reacts with the bromine.



Ethene *Bromine (brownish red)* *1,2-Dibromoethane (colorless)*

Another important addition reaction of the alkenes is that with water. This reaction, called *hydration*, requires the presence of a mineral acid, such as sulfuric acid (H_2SO_4), as a catalyst.



Ethene *Water* *Ethyl alcohol*

Vast quantities of ethyl alcohol, for use as an industrial solvent, are made from ethylene. This alcohol is structurally identical to that used in alcoholic beverages. However, federal law requires that all drinking alcohol be produced by the natural process called fermentation (chapter 16).

The most important alkene reaction of all, perhaps, is polymerization. This topic will be discussed in chapter 21.

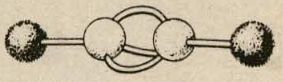


Figure 14.11 Ball-and-stick model of acetylene.

14.12 Triple Tight: The Alkyne Series

In alkenes carbon atoms in the double bond share two pairs of electrons. Carbon atoms can also share three pairs of electrons, forming triple bonds. Compounds containing such bonds are called *alkynes*. The common name of the simplest alkyne is acetylene (C_2H_2). Its structure is

$$H{-}C{\equiv}C{-}H$$

About 10% of all acetylene produced is used in oxyacetylene torches for cutting and welding metals. The flame from such a torch can attain a very high temperature. Most acetylene, however, is converted to chemical intermediates which are in turn used to make vinyl and acrylic plastics, fibers, and resins and a variety of other chemical products. It is even incorporated as a part of the molecular architecture of birth control pills (chapter 27).

The alkynes are similar to the alkenes in both physical and chemical properties. For example, they undergo many of the typical addition reactions of alkenes. Like ethene, acetylene has been used as an anesthetic for surgery. At higher concentrations, it causes narcosis and asphyxia. The IUPAC nomenclature for alkynes parallels that of the alkenes, except that the family ending is *-yne* rather than *-ene*. The official name for acetylene is ethyne. Notice that the ending of the common name, acetylene, is deceptive. It sounds very much like ethylene or propylene. Remember that acetylene is an alkyne and that ethylene and propylene are alkenes.

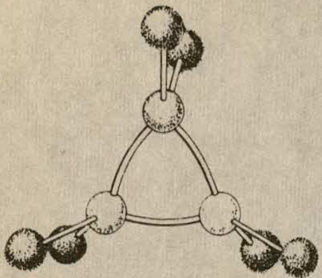
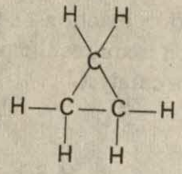


Figure 14.12 Ball-and-stick model of cyclopropane.

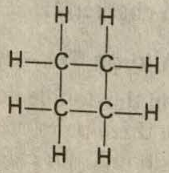
14.13 On Rings and Things: Cycloalkanes

The hydrocarbons we have encountered so far have been composed of open-ended chains of carbon atoms. Carbon and hydrogen atoms can also hook up in other arrangements, some of them quite interesting. There is a synthetic hydrocarbon which has the formula C_3H_6. The three carbons are joined in a *ring*, or *cycle*. The compound is called cyclopropane.



In addition to having an interesting structure, cyclopropane has some intriguing properties. It is an excellent anesthetic, for when inhaled it renders the patient unconscious and unaware of pain. It is also explosive when mixed with air; thus, care must be taken to exclude the possibility of a flame or spark from the operating room when this material is in use.

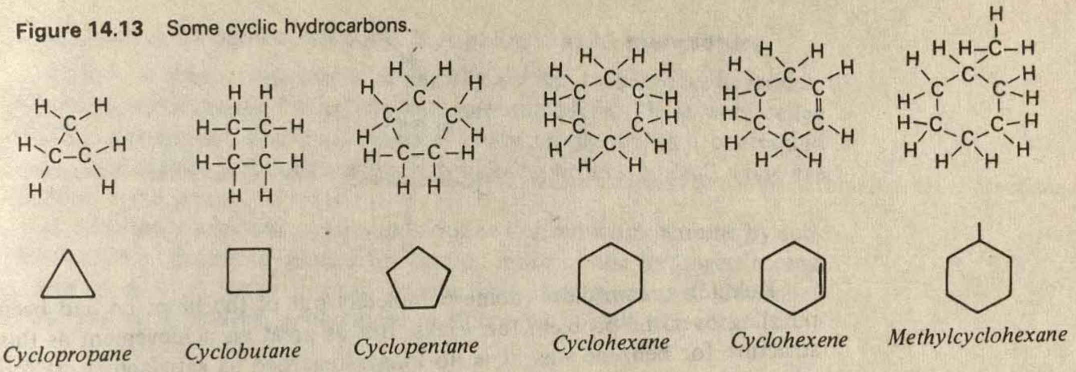
Names of cycloalkanes are formed by addition of the prefix *cyclo-* in front of the name of the open-chain compound with the same number of carbon atoms as are in the ring. Thus, the name for the compound



is cyclobutane. Names and structures of several cycloalkanes are given in **figure 14.13.** Note that the carbon atoms of each compound form a regular geometric figure. For example, the three carbon atoms of cyclopropane form a triangle. Therefore, a triangle is frequently used to represent cyclopropane. Similarly, the five carbons of cyclopentane form a pentagon, and we use a pentagon to represent cyclopentane. It is understood that the carbon atoms occur at the angles of the particular figure and that each carbon atom is attached to sufficient hydrogens to give the carbon atom four bonds. Cyclic compounds may also contain attached substituent groups (see **figure 14.13**).

The physical, chemical, and physiological properties of these cyclic hy-

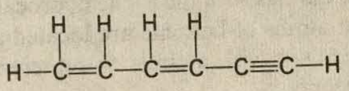
Figure 14.13 Some cyclic hydrocarbons.



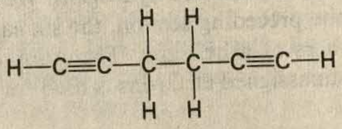
drocarbons are generally quite similar to those of the corresponding open-chain compounds. Cycloalkanes (with the exception of cyclopropane) act very much like ordinary alkanes. Cycloalkenes, like other alkenes, undergo addition reactions. Cyclic hydrocarbons with five- and six- membered rings occur in petroleum from certain areas; California crude, for instance, is particularly rich in these compounds. Like all other hydrocarbons, cyclic hydrocarbons burn.

14.14 Of Benzene . . . and Dozing by the Fire

Still another type of hydrocarbon is represented by the compound benzene. Benzene was first isolated in 1825 from a by-product of whale oil by Michael Faraday. (This is the same Michael Faraday whose electrolysis experiments were described in chapters 2 and 12.) The molecular formula of benzene was soon (in 1834) determined to be C_6H_6. One can write many structures corresponding to the formula C_6H_6. Two possible structures are shown here. All of these follow the valence rules; that is, each carbon atom has four bonds and each hydrogen has one bond.



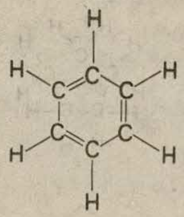
$$\mathrm{H{-}\overset{H}{\overset{|}{C}}{=}\overset{H}{\overset{|}{C}}{-}\overset{H}{\overset{|}{C}}{=}\overset{H}{\overset{|}{C}}{-}C{\equiv}C{-}H}$$



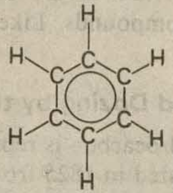
$$\mathrm{H{-}C{\equiv}C{-}\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}{-}\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}{-}C{\equiv}C{-}H}$$

The real substance, benzene, didn't have the properties that one would predict from these structures (and many others that were proposed). For example, if benzene's structure really were one of the above, it would be expected to undergo addition reactions readily. It does not.

It wasn't until 1865 that Friedrich August Kekulé, a German chemist, proposed a widely accepted structure for benzene. One day, while dozing by the fire, he saw chains of atoms whirling in a dance. Suddenly, one of the "snakes" seized its own tail, forming a swirling ring. Until Kekulé's vision, chemists had thought only of chains of carbon atoms. Now they could envision rings of atoms as well. (Cyclopropane, mentioned earlier here, was not prepared until 1881.) Kekulé proposed this structure for benzene.

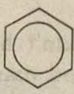


Kekulé's dream didn't come completely out of the blue; he had been puzzling over the problem for weeks. But as great an achievement as this structure for benzene was, it is no longer regarded as satisfactory. It too represents a compound which should readily enter addition reactions. Modern chemists, using quantum mechanics, realize that, in order for benzene to behave as it does, the "extra" or double-bond electrons can't be located between specific carbon atoms but must be shared equally by all six carbon atoms. Now the structure of benzene is often rendered as

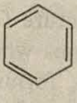


where the circle represents the six "extra" electrons. There are no real double bonds but a very stable ring of electrons, which resists being disrupted. Benzene doesn't enter addition reactions because this would destroy the ring of electrons.

It takes a good deal of time to draw out structures for benzene showing all the carbons and hydrogens. We note that, as with the cyclic hydrocarbons in the preceding section, the six carbon atoms of benzene are located at the corners of a hexagon. Therefore, a hexagon with a circle to represent the six unassigned electrons is used for benzene.



The Kekulé structure is still found in many texts.

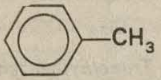


Remember that the above structures are not really benzene (a gasoline-like liquid which boils at 80 °C). No one has ever seen a benzene molecule. The structure represents a *concept* of the benzene molecule.

14.15 Aromatic Hydrocarbons: Structure and Nomenclature

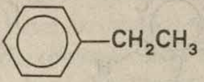
There are many compounds chemically similar to benzene. Several of those discovered in the early days had pleasant odors. These were called *aromatic compounds*. The label *aromatic* today simply means a compound related to benzene and does not imply a pleasing aroma. In fact, some are odorless. Others stink.

A number of aromatic compounds can be derived from benzene by substitution of a variety of groups for one or more of the hydrogen atoms. Substitution of a methyl group for one hydrogen gives methylbenzene, better known as *toluene* (pronounced to rhyme with "doll, you mean").



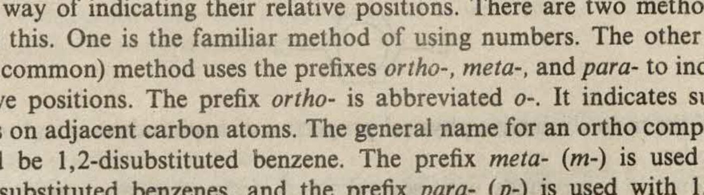
Remember that in this formula those points which are not shown attached to a substituent carry a hydrogen atom. Toluene is an important solvent and a starting material for the synthesis of other aromatic compounds.

Substitution of an ethyl group for a hydrogen atom gives ethylbenzene.



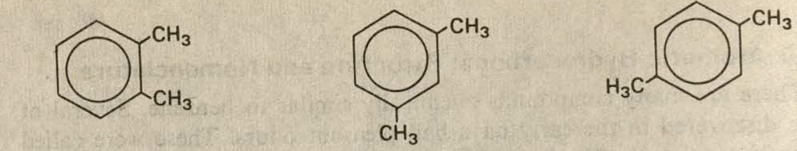
This compound is an important intermediate in the synthesis of styrene, from which the common plastic polystyrene is made (chapter 21).

When two substituents are attached to the benzene ring, we must use some way of indicating their relative positions. There are two methods of doing this. One is the familiar method of using numbers. The other (and more common) method uses the prefixes *ortho-*, *meta-*, and *para-* to indicate relative positions. The prefix *ortho-* is abbreviated *o-*. It indicates substituents on adjacent carbon atoms. The general name for an ortho compound would be 1,2-disubstituted benzene. The prefix *meta-* (*m-*) is used with 1,3-disubstituted benzenes, and the prefix *para-* (*p-*) is used with 1,4-disubstituted benzenes. All four of the following structures represent the *same* compound, *m*-dinitrobenzene (NO_2 is called the *nitro* group).



For three or more substitutents, the numbering system must be used. Examples are shown in **figure 14.14.**

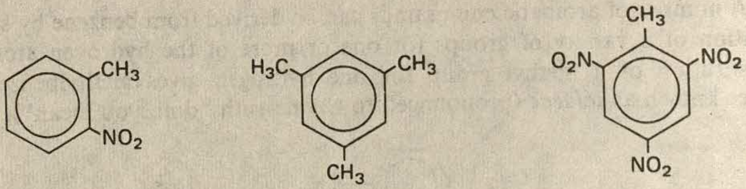
In another group of aromatic hydrocarbons, two or more benzene rings are "fused" together; that is, the rings have two or more carbon atoms in common. The simplest of these is naphthalene ($C_{10}H_8$).



o-*Xylene* *(1,2-dimethylbenzene)*

m-*Xylene* *(1,3-dimethylbenzene)*

p-*Xylene* *(1,4-dimethylbenzene)*

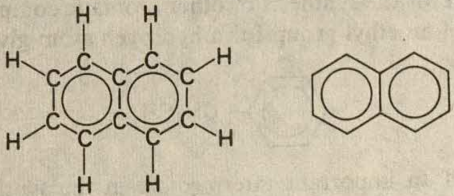


o-*Nitrotoluene* *(2-nitrotoluene)*

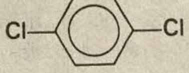
1,3,5-Trimethylbenzene

2,4,6-Trinitrotoluene *(TNT)*

Figure 14.14 Some aromatic hydrocarbons and derivatives.

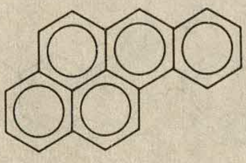


Naphthalene has been used as a moth repellant, as has *p*-dichlorobenzene.



One of the most distinctive physical properties of naphthalene is its "mothball" odor.

Aromatic compounds with several fused rings often are *carcinogenic,* that is, they can induce cancer. Typical of these compounds is 3,4-benzpyrene (benz[a]pyrene).



This compound is known to induce cancer in laboratory animals. It is found in cigarette smoke and automobile exhaust fumes.

14.16 Properties of Aromatic Hydrocarbons

Benzene, toluene, and the xylenes are liquids at room temperature. The compounds involving fused rings, the *polycyclic* hydrocarbons, are solids.

One possible problem that may arise as we "get the lead out" of gasoline, according to some research scientists, is an increase in the amount of 3, 4-benzpyrene in exhaust fumes. Burning of any gasoline produces some of this compound. However, to increase the octane rating of lead-free gasoline, researchers added more aromatic hydrocarbons to the mixture. Some scientists fear that these aromatics will lead to increased concentrations of cancer-producing polycyclic aromatic hydrocarbons in automobile exhausts.

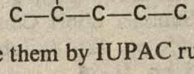
All are insoluble in water. They are generally soluble in organic solvents such as hexane.

Aromatic hydrocarbons, like all the hydrocarbons, burn. They also enter into a number of reactions of great interest to chemists. For now, however, we shall concentrate on their physiological properties.

Most of the aromatic hydrocarbons present toxic hazards. Benzene, whether inhaled or ingested, may cause convulsions or even death by respiratory failure. Chronic exposure to lower levels of benzene can depress the formation of blood cells by bone marrow. Prolonged chronic exposure can cause death. Once (and to some extent still) extremely popular as a laboratory solvent, benzene is now being replaced in many instances by toluene, which is somewhat less toxic. Toluene does act as a narcotic in high concentrations, but the body can metabolize and excrete small amounts of toluene. The methyl group on toluene offers the body a "handle" on which to work. Benzene does not have this "handle." The xylenes are similar to toluene in their physiological properties. As we have seen, many of the polycyclic aromatic hydrocarbons are carcinogenic. All aromatic compounds should be handled only after adequate evaluation of the hazards involved. Volatile solvents such as benzene and toluene should certainly be used only with adequate ventilation.

Problems

1. List three characteristics of the carbon atom that make possible the existence of millions of organic compounds.
2. List three ways in which a "typical" organic compound differs from a "typical" inorganic one.
3. Define, illustrate, or give an example for each of these terms.
   a. hydrocarbons
   b. alkane
   c. paraffin
   d. saturated
   e. unsaturated
   f. substituent
   g. alkene
   h. alkyl group
   i. alkyne
   j. homologous series
   k. isomer
   l. geometric isomerism
   m. aromatic compound
4. Write structures for the five isomeric hexanes (C_6H_{14}). Name each by the IUPAC system.
5. Including geometric isomers, there are five isomeric hexylenes with this basic carbon skeleton.



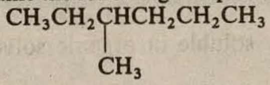
$$C-\overset{\overset{\displaystyle C}{|}}{C}-C-C-C$$

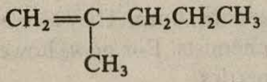
Draw all five isomers and name them by IUPAC rules.

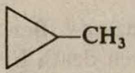
6. Write structures for the following.
   a. isopentane
   b. 4-ethyl-3-methyloctane

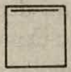
c. 2,2,5-trimethylhexane
d. propylene
e. 3-ethyl-2-pentene
f. 3-*tert*-butyl-1-hexene
g. *cis*-2-hexene
h. *trans*-3-hexene
i. acetylene
j. 1-butyne
k. toluene
l. *p*-dichlorobenzene
m. naphthalene
n. *m*-diethylbenzene
o. 2,4-dinitrotoluene
p. 1,2,4-trimethylbenzene
q. cyclohexane
r. cyclopentene

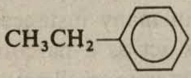
7. Name the following compounds by the IUPAC system.

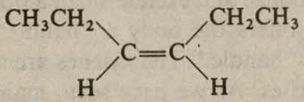
a.

$CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2CH_3$

b.

$CH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}CH_2CH_2CH_3$

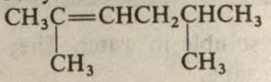
c.


d.


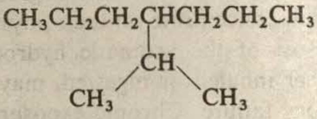
e.


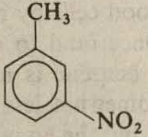
f.


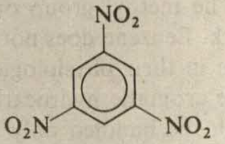
g. $CH_3CH_2CH_2C{\equiv}C{-}H$

h.

$CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CHCH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$

i. $CH_3C{\equiv}CCH_3$

j.


k.


l.


8. Write equations for the following.
   a. the complete combustion of propane
   b. the hydrogenation of propene
   c. the addition of bromine to isobutylene (methylpropene)
   d. the hydration of ethene
9. What is the danger in swallowing liquid alkanes?
10. What physiological effect does cyclopropane exhibit which is not shared by the other cycloalkanes?
11. Distinguish between lighter and heavier liquid alkanes in terms of their effect on the skin.
12. Name a physiological effect of some polycyclic aromatic hydrocarbons.

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4. Noller, Carl R., *Chemistry of Organic Compounds*, 3rd ed., Philadelphia: W. B. Saunders, 1965. Is a bit out of date but still an excellent source.
5. Westheimer, Frank H., "Summer Short Course in Organic Chemistry, Parts I–IV," *Chemistry*, June 1965, pp. 12–18; July 1965, pp. 10–16; August 1965, pp. 18–19; September 1965, pp. 21–24.
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chapter 15

Halogenated Hydrocarbons

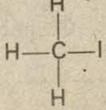
Human beings seem to have a greater liking for halogens in their organic compounds than does nature itself. Very few halogen-containing organic compounds occur in nature, but chemists have created a dazzling variety of such compounds. And the general public has come to depend on a large number of these. Medicines, building materials, farm products, and a myriad of convenience products incorporate the halogen-carbon combination.

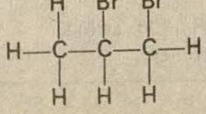
As each passing year demonstrates, nature can get quite upset over our attempts to correct its deficiencies. The environmental and health hazards posed by the sudden influx of synthetic materials have proven to be highly significant. Unfortunately, the answer to the problem is not simply a matter of stopping all production of synthetic compounds—not unless we are willing to put up with dramatic increases in pestilence, disease, and famine. What, then, is the answer? It is the same as for any difficult problem—to take a cold, hard look at what we gain and what we lose in each case, to weigh these against one another, and then to retain, eliminate, or modify the materials on the basis of the balance.

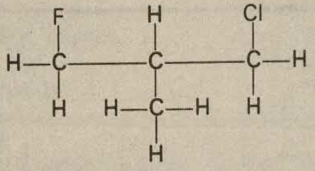
We shall consider some huge halogen-containing molecules in chapter 21. For now, we'll concentrate on some smaller ones.

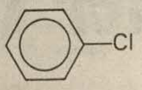
15.1 Alkyl Halides: Structure and Nomenclature

In general, halogenated hydrocarbons are compounds in which one or more hydrogens of a hydrocarbon have been replaced by halogen atoms. The halogen may be fluorine (F), chlorine (Cl), bromine (Br), or iodine (I). Each of the following is a halogenated hydrocarbon, or a halocarbon.









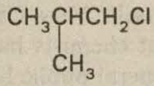
More specifically, replacement of one hydrogen atom of an alkane with a halogen gives an *alkyl halide*. These compounds are given common names which consist of two parts. The first is the name of the alkyl group; the second is the stem of the name of the halogen, with the ending *-ide*. Refer back to **table 14.3** for a list of the common alkyl groups.

Example 15.1 What is the common name for the compound with this formula?

$$CH_3CH_2Br$$

The alkyl group (CH_3CH_2—) is ethyl. The halogen is bromine. The compound is therefore ethyl bromide.

Example 15.2 What is the common name for this compound?



$$\underset{CH_3}{CH_3\underset{|}{C}HCH_2Cl}$$

The alkyl group is isobutyl. The halogen is chlorine. The compound is named isobutyl chloride.

Table 15.1
Some alkyl halides

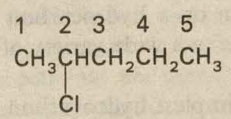
Compound	*Structure*	*Boiling Point (in degrees Celsius)*	*Uses*
Methyl chloride	CH_3Cl	−24	Refrigerant; chemical intermediate for manufacturing of silicones, methyl cellulose, and so on
Methyl bromide	CH_3Br	4	Poison gas for insect and rodent control
Ethyl chloride	CH_3CH_2Cl	13	Intermediate for synthesis of tetraethyl lead; local anesthetic; emergency general anesthetic
n-Butyl chloride	$CH_3CH_2CH_2CH_2Cl$	79	Intermediate for synthesis of butyl cellulose; killing of intestinal worms in dogs
Pentyl chlorides	$C_5H_{11}Cl$ (various isomers)	—	Chemical intermediates

Sometimes we may wish to speak of alkyl halides in general. Sometimes (later on in this book) we may wish to refer to other kinds of compounds which contain alkyl groups without bothering to indicate a specific alkyl group. In these instances, we represent the alkyl group by the letter *R*, as in R—Cl, (read "alkyl chloride"). The *R* stands for any alkyl group—methyl, ethyl, isopropyl, whatever.

Names, structures, properties, and uses of some common alkyl halides are given in **table 15.1.**

The IUPAC system differs from the common nomenclature in that halogen substituents are indicated by the prefixes *fluoro-, chloro-, bromo-,* and *iodo-*. The prefix is used with the name of the parent alkane, with numbers to indicate the position of the halogen if necessary.

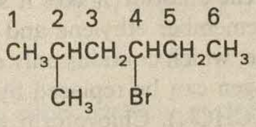
Example 15.3 Give the IUPAC name for



$$\overset{1}{\mathrm{CH_3}}\underset{\substack{|\\ \mathrm{Cl}}}{\overset{2}{\mathrm{C}}}\mathrm{H}\overset{3}{\mathrm{CH_2}}\overset{4}{\mathrm{CH_2}}\overset{5}{\mathrm{CH_3}}$$

The parent alkane is pentane. The name of the compound is 2-chloropentane.

Example 15.4 Give the IUPAC name for

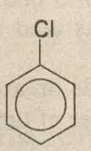


$$\overset{1}{\mathrm{CH_3}}\underset{\substack{|\\ \mathrm{CH_3}}}{\overset{2}{\mathrm{C}}}\mathrm{H}\overset{3}{\mathrm{CH_2}}\underset{\substack{|\\ \mathrm{Br}}}{\overset{4}{\mathrm{C}}}\mathrm{H}\overset{5}{\mathrm{CH_2}}\overset{6}{\mathrm{CH_3}}$$

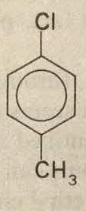
The parent alkane is 2-methylhexane. The compound is named 4-bromo-2-methylhexane.

15.2 Aryl Halides: Structure and Nomenclature

Just as alkyl halides are derived from alkanes, aryl halides are derived from aromatic hydrocarbons. As for alkyl halides, it is occasionally useful to have a general formula for compounds with halogen attached to an aromatic ring. For this purpose chemists use the symbol *Ar*, which stands for the *aryl* group. An aryl halide is any compound in which a halogen is attached directly to an aromatic ring. For example, all of the following are aryl chlorides.



or



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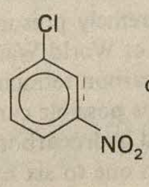
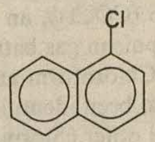
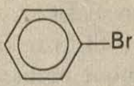
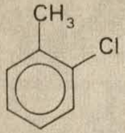


or

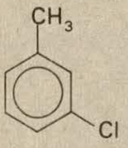


Replacement of one of the hydrogen atoms of benzene with a bromine atom gives bromobenzene (C_6H_5Br).

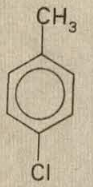




2-Chlorotoluene
(o-chlorotoluene)



3-Chlorotoluene
(m-chlorotoluene)



4-Chlorotoluene
(p-chlorotoluene)

Replacement of a hydrogen atom attached to the toluene ring with chlorine gives one of three isomeric chlorotoluenes. These names assume the methyl group of toluene to be on the first carbon atom of the ring.

Chlorobenzene (whose boiling point is 132 °C) and *o*-chlorotoluene (whose boiling point is 159 °C) both find some use as solvents, particularly where a liquid with a high boiling point is desired. All are fairly important as chemical intermediates. For example, chlorobenzene is used in the production of aniline (chapter 19), phenol (chapter 16), and DDT (section 15.8).

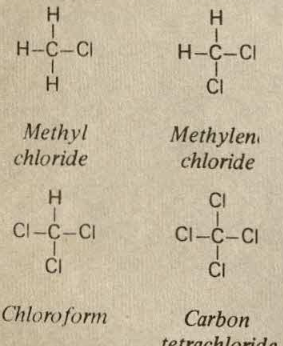
15.3 Polyhalogenated Hydrocarbons: Structure, Nomenclature

More than one hydrogen on a hydrocarbon molecule can be replaced by halogen atoms. This leads to a wide variety of interesting and often useful compounds.

Consider methane, the simplest hydrocarbon. One hydrogen can be replaced by chlorine, yielding methyl chloride (section 15.1). A second hydrogen can be substituted to yield dichloromethane or methylene chloride (CH_2Cl_2). This compound is a common solvent. It boils at 40 °C; hence, it can easily be removed by distillation if one wishes to recover the solute. Although the name methylene chloride makes it sound like the compound contains a double bond (remember ethylene and propylene?), there is no double bond in the molecule, which contains only one carbon atom.

A third methane hydrogen can be replaced by chlorine, giving chloroform or trichloromethane ($CHCl_3$). Chloroform was one of the first anesthetics and was once widely used. It has been largely replaced by safer, less toxic chemicals. Chloroform is still an important commercial and industrial solvent.

Figure 15.1 The chlorine derivatives of methane.



Methyl chloride

Methylene chloride

Chloroform

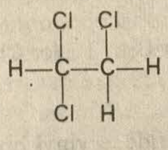
Carbon tetrachloride

Replacing all four of methane's hydrogens with chlorine gives carbon tetrachloride (CCl_4), also called tetrachloromethane. Carbon tetrachloride has been used as a dry-cleaning solvent and in fire extinguishers. It is no longer recommended for either use. Exposure to carbon tetrachloride (or most of the other chlorinated hydrocarbons, for that matter) can cause severe damage to the liver. Even the vapor, breathed in small amounts, can cause serious illness if the exposure is prolonged. Use of a carbon tetrachloride fire extinguisher in conjuction with water to put out a fire can be deadly. Carbon tetrachloride reacts with water at high temperatures to form phosgene ($COCl_2$), an extremely poisonous gas. In fact, phosgene was used in the poison gas battles of World War I.

Chloroform and carbon tetrachloride have, through tests made on animals, been identified as possible carcinogens. It seems only a matter of time until other chlorinated hydrocarbons are so identified also.

With ethane, from one to six hydrogen atoms can be replaced by chlorine. Replacement of only one hydrogen gives ethyl chloride (section 15.1). Replacement of two hydrogens can give either of two isomers. 1,2-Dichloroethane is commonly used as a solvent, particularly for rubber.

Replacement of three of the hydrogen atoms of ethane with chlorine atoms also gives two isomers (shown in margin). The structure

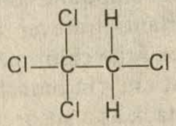


also represents 1,1,2-trichloroethane. Let us again remind you that formulas that look somewhat different do not always represent different compounds. Both of the trichloroethanes are used as commercial and industrial solvents. 1,1,1-Trichloroethane is used for the cleaning of molds used in the fabrication of plastics.

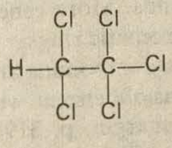
Replacement of four hydrogens of ethane with chlorine also leads to isomers. Only one is of importance, however—1,1,2,2-tetrachloroethane. This compound is widely used but highly toxic. It dissolves rubber, cellulose acetate, and other complex organic materials. It is also used to sterilize soil and as a component of weed killers and insecticide preparations.

Example 15.5 How many isomeric tetrachloroethanes are there? How many pentachloroethanes are there? Write the structures and give IUPAC names for each isomer.

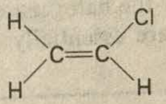
There are only two tetrachloroethanes, 1,1,2,2-tetrachloroethane (shown in margin) and 1,1,1,2-tetrachloroethane,



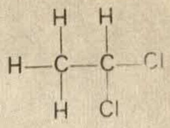
There is only one possible pentachloroethane (hence, pentachloroethane is the IUPAC name and it is not necessary to use numbers to indicate a form).



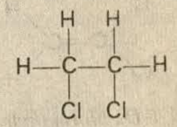
Chlorinated compounds can also contain doubly bonded carbons. Replacement of one hydrogen of ethylene with chlorine gives a compound called vinyl chloride.



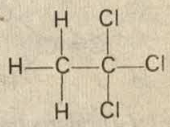
The IUPAC name for this compound is chloroethene. Its common name is patterned after that of the alkyl halides—the carbon portion is named as



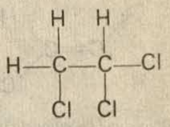
1,1-Dichloroethane



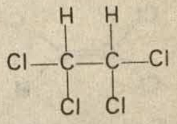
1,2-Dichloroethane



1,1,1-Trichloroethane

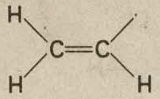


1,1,2-Trichloroethane

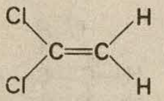


1,1,2,2-Tetrachloroethan

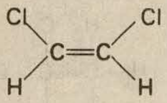
a substituent and the halogen as a halide. Vinyl is the name given to the carbon group



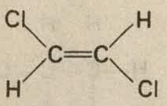
(or $CH_2{=}CH—$)



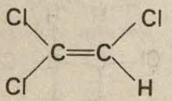
1,1-Dichloroethylene
(1,1-dichloroethene)



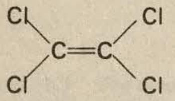
cis-*1,2-Dichloroethylene*
*(*cis-*1,2-dichloroethene)*



trans-*1,2-Dichloroethylene*
*(*trans-*1,2-dichloroethene)*



Trichloroethylene



Tetrachloroethylene

There exist also a vinyl fluoride, a vinyl bromide, and a vinyl iodide, but it is vinyl chloride that has had the most significant impact on our society. It is the starting material for the synthesis of the important plastic poly(vinyl chloride), the "vinyl" one finds on seat covers, in phonograph records, in house sidings, and in many other places (chapter 21). In January 1974, B. F. Goodrich Company announced that three workers who cleaned reactors in which the poly(vinyl chloride) was prepared had died of angiosarcoma, a rare form of liver cancer. During the following months, other cases were reported and evidence was presented which linked the malignancy to long-term (20 to 30 years' duration), high-level exposure to vinyl chloride and not to the plastic itself. The plastics industry and the government undertook the establishment of safety guidelines for industrial workers engaged in operations involving the gaseous vinyl chloride. It was recommended that a safe breathing atmosphere be considered one for which tests revealed no detectable level of the gas.

Replacement of two hydrogens of ethylene gives three isomers which, like most smaller halogenated compounds, are generally referred to by their common names. More important, however, is the trichloro derivative. This is one of the most important of the chlorinated hydrocarbon solvents. It is used as a dry-cleaning solvent and (in industry) for degreasing metal parts. It has recently come under attack as a suspected carcinogen.

Tetrachloroethylene (also called perchloroethylene*) is also used as a dry-cleaning solvent, particularly for synthetic fabrics.

All of the above polyhalogenated compounds, whether they contain double bonds or not, are referred to as *aliphatic* compounds to distinguish them from *aromatic* compounds. More generally, aliphatic compounds are those which do not contain aromatic rings.

Polyhalogenated aromatic compounds are also commonly encountered. Replacement of two hydrogens of benzene with chlorine gives three isomeric dichlorobenzenes (shown in margin, p. 319). *p*-Dichlorobenzene has been used to protect garments from the larvae of the clothes moth and to protect peach trees from borer larvae.

15.4 Physical Properties of the Halogenated Hydrocarbons

The physical properties of the halogenated hydrocarbons are much like those of the alkanes. Most are essentially insoluble in water. Generally,

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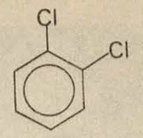
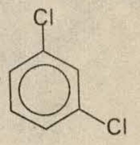
*The prefix *per-* indicates the maximum substitution. In perhalo compounds, all hydrogens have been replaced by halogen atoms.

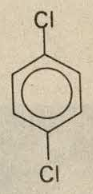
they are good solvents for other organic compounds such as fats, greases, oils, waxes, resins, and for some plastics and elastomers (chapter 21).



o-*Dichlorobenzene*
(1,2-dichlorobenzene)



m-*Dichlorobenzene*
(1,3-dichlorobenzene)



p-*Dichlorobenzene*
(1,4-dichlorobenzene)

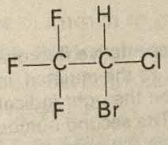
Monofluoro and monochloro compounds are less dense than water, but monobromo and monoiodo compounds with only a few carbon atoms are denser than water (in contrast to the hydrocarbons). Polyhalogenated hydrocarbons are generally denser than water. Chloroform and carbon tetrachloride, for example, have densities of 1.5 g/ml and 1.6 g/ml, respectively.

The boiling points of many chlorinated hydrocarbons are close to those of alkanes of comparable molecular weight. For example, the boiling point of ethyl chloride (which has a molecular weight of 64.5) is 13 °C, between that of butane (whose molecular weight is 58.0 and whose boiling point is 0 °C) and pentane (whose molecular weight is 72 and whose boiling point is 36 °C). Chlorobenzene (with a molecular weight of 112.5) boils at 132 °C, while ethylbenzene (with a molecular weight of 106.0) boils at 136 °C. As with most of our general rules, there are many exceptions to this one, but the correlation between the boiling points of these two classes of compounds is worthy of comment. Boiling points reflect the strength of the forces holding the molecules of a liquid together. For compounds of comparable molecular weight, the higher the boiling point, the stronger the forces of attraction between molecules. Since carbon-chlorine bonds are polar, it may seem surprising that the interaction of these dipoles doesn't result in higher boiling points for the chlorinated hydrocarbons. Recall, however, that dispersion forces for larger molecules can be more important than dipole forces (section 7.4) and that most liquids which have high boiling points and which are composed of small molecules are associated by hydrogen bonding.

Physical properties, particularly solubility and volatility, determine to a large extent where halogenated hydrocarbons go in our bodies—and what they do when they get there.

15.5 Halogenated Hydrocarbons: Physiological Properties

As in their physical properties, the halogenated hydrocarbons are much like the alkanes in their physiological properties. Gaseous compounds—and vapors of volatile liquids—often act as anesthetics. Chloroform (section 15.3) is an effective anesthetic. It is powerful and fast acting. It has the advantage (over ether and cyclopropane) of being nonflammable. Unfortunately, however, the effective dose for anesthesia is quite near the lethal dose. It is seldom used these days on humans. It was largely replaced by 2-bromo-2-chloro-1,1,1-trifluoroethane (also called halothane), which shares the advantages of chloroform.



$$\begin{array}{ccccc} & \mathrm{F} & & \mathrm{H} & \\ & | & & | & \\ \mathrm{F}- & \mathrm{C} & - & \mathrm{C} & -\mathrm{Cl} \\ & | & & | & \\ & \mathrm{F} & & \mathrm{Br} & \end{array}$$

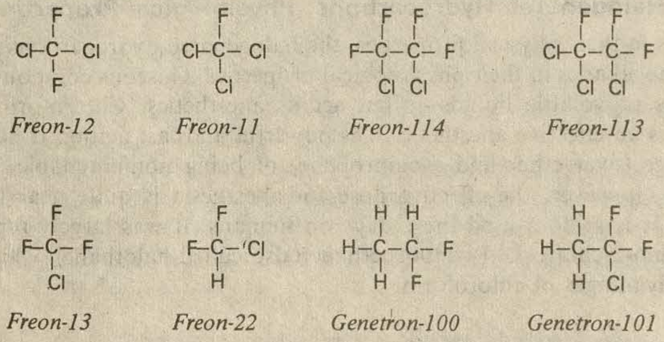
The safety of this replacement with regard to toxicity, particularly for the workers in the operating room, has recently been questioned.

Some halogenated hydrocarbons are narcotic in high concentrations, perhaps accounting for the abuse of some of these compounds by glue sniffers. Such use is exceedingly dangerous. Aside from the hazard of immediate death, repeated exposure to these compounds often leads to extensive damage to the liver and kidneys.

On the skin, liquid halogenated hydrocarbons can cause dermatitis by washing away natural oils. Some are particularly irritating to the skin or to the eyes, the mucosa, or the respiratory tract. Many are readily absorbed through the skin, and spills on the skin can ultimately lead to liver damage. As we indicated in section 15.3, one halogenated hydrocarbon, vinyl chloride, has been implicated as the cause of a liver cancer. No halogenated hydrocarbon should be used without a proper evaluation of the hazards. If no warning is given on the label, look up the properties in a reference such as *The Merck Index* (reference 16).

15.6 Fluorinated Hydrocarbons: Refrigerants, Aerosol Spray, and the Ozone Layer

In the remainder of this chapter we will discuss halogenated hydrocarbons of particular concern to those of us who are interested in the environment and in human health. That, no doubt, includes almost everyone. Before we start, let us propose an approach to reading the remaining sections. You will encounter a number of quite complicated structures, the kind that always bring to mind the question "How many of these will I have to memorize?" The structures are not there to be memorized but to illustrate a point. Read them as you would the text. (How many paragraphs of this book have you memorized?) Observe the similarities or differences which are pointed out, but don't allow the details of the compounds to disconcert you. The primary point is that these are all halogenated organic compounds and they have had a profound effect on all of us.



$\mathrm{Cl{-}\overset{F}{\underset{F}{C}}{-}Cl}$ *Freon-12*

$\mathrm{Cl{-}\overset{F}{\underset{Cl}{C}}{-}Cl}$ *Freon-11*

$\mathrm{F{-}\overset{F}{\underset{Cl}{C}}{-}\overset{F}{\underset{Cl}{C}}{-}F}$ *Freon-114*

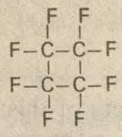
$\mathrm{Cl{-}\overset{F}{\underset{Cl}{C}}{-}\overset{F}{\underset{Cl}{C}}{-}F}$ *Freon-113*

$\mathrm{F{-}\overset{F}{\underset{Cl}{C}}{-}F}$ *Freon-13*

$\mathrm{F{-}\overset{F}{\underset{H}{C}}{-}Cl}$ *Freon-22*

$\mathrm{H{-}\overset{H}{\underset{H}{C}}{-}\overset{H}{\underset{F}{C}}{-}F}$ *Genetron-100*

$\mathrm{H{-}\overset{H}{\underset{H}{C}}{-}\overset{F}{\underset{Cl}{C}}{-}F}$ *Genetron-101*



Freon-C318

Figure 15.2 Some representative fluorocarbons. The *Freon* code numbers, to the initiated, indicate the formula. The number on the right indicates the number of fluorine atoms. The second number from the right is one more than the number of hydrogers. The third number from the right is one less than the number of carbons. *Genetron* obviously uses a different code.

A group of fluorocarbons, most of which also contain chlorine, were widely used as the dispersing gas in aerosol cans and are used as refrigerants in air conditioners and refrigerators. They are generally known as "freons," although the word *Freon* is actually a trade name of the Du Pont Company. Other chlorofluorocarbons are sold under trade names such as *Genetron* (Allied Chemical Company), *Isotron* (Pennwalt Corporation), and *Ucon* (Union Carbide).

Figure 15.3 F. S. Rowland.

The two most important chlorofluorocarbons are dichlorodifluoromethane (Freon-12) and trichlorofluoromethane (Freon-11). Both were produced in quantities of over a billion kilograms each per year. Structures of these and other "freons" are shown in **figure 15.2.**

For many years, the chlorofluorocarbons were thought to be both chemically nonreactive and physiologically inert. It was this property which encouraged such widespread use. Only in the last few years has their safety really been questioned. In the late 1960s incidents involving young people who sought "kicks" by inhaling aerosol sprays set off investigations. Several youngsters died from this bizarre form of drug abuse, the victims of heart failure. The same chlorofluorocarbons (mainly Freon-11 and Freon-12) that were producing the intoxicating effect were stopping their hearts. Consumer groups began to question their safety for everyday use. The Center for Science in the Public Interest (SIPI) denounced aerosol preparations as potential bombs, because the pressurized containers may explode when exposed to heat. The Health Research Group questioned the safety of the propellants in aerosol spray cans, particularly for those with asthma or heart disease. Others denounced aerosols as a giant rip-off. The products are generally available at lower prices in other forms. "What price convenience?" they asked, with obvious reference to health effects as well as to cost.

On the other side of the coin, industry spokespersons could point to 20 years' use as an indication of safety. Deaths and injuries could invariably be traced to product abuse or gross misuse with failure to follow directions. Nonetheless, some products have been removed from the market, and investigations of potential dangers continue.

Figure 15.4 Is the ozone layer being destroyed by chlorofluorocarbon propellants? (Courtesy of the Natural Resources Defense Council, Inc., New York.)

Further controversy regarding the chlorofluorocarbons arose in 1974. F. Sherwood Rowland, a chemist at the University of California at Irvine, questioned the effect of these compounds on the earth's protective ozone layer. He speculated that, because of their inertness to ordinary chemical reagents, chlorofluorocarbons may be making their way up through the atmosphere to the stratosphere. There they may well react with atomic oxygen and ultraviolet light to form chlorine atoms, which catalyze the decomposition of ozone. This reaction has been known to occur in the laboratory under conditions simulating those in the stratosphere. In partial confirmation of Rowland's speculations, chlorofluorocarbons have been detected in the stratosphere. Their effect on the ozone layer has yet to be proven. The risk is rather great. The National Academy of Sciences estimates that a 10% decrease in the thickness of the ozone layer would cause an increase of 8000 cases of skin cancer per year among the light-skinned population of the United States.

15.7 How DDT Won the War and Lost the Battle

Since the earliest days of recorded history (and surely even before that) people have been plagued by insect pests. Three of the biblical plagues of Egypt (described in the Book of Exodus) were insect plagues: lice, flies, and locusts. The decline of Roman civilization has been attributed in part to malaria, a mosquito-borne disease that destroys vigor and vitality when it does not kill. Bubonic plague, carried by rats (and by fleas from rats to humans), swept the Western world repeatedly during the Middle Ages. One such plague (occurring in the 1660s) is estimated to have killed 25 million people—one-fourth the population of Europe. The first attempt to dig the Panama Canal (by the French in the 1880s) was defeated by malaria.

Diligent use of modern chemical pesticides may be the only thing that stands between us and some of these insect-borne plagues. Chemical pesticides also prevent consumption of a major portion of our foodstuffs by insects and other pests.

People have long tried to control insect pests by draining swamps, pouring oil on ponds (to kill mosquito larvae), and using a variety of chemicals. Most of these chemicals were compounds of arsenic (As). A few, such as pyrethrum (used in mosquito control) and nicotine sulfate (Black Leaf 40), are obtained from plant sources. Lead arsenate [$Pb_3(AsO_4)_2$] is a particularly effective poison, because both the lead and arsenic in it are toxic.

Most of these are extremely poisonous* to people and other animals, as well as to insects (**table 15.2**). They should more properly be called biocides rather than insecticides. As little as 40 mg of nicotine is fatal to human beings.

The discovery of the insecticidal properties of DDT was made in Switzerland by Paul Müller shortly before World War II. The compound was tested in Europe and was found to be quite effective against certain vine grape pests and against a particularly bad infestation of potato beetles. When the war came, the supply of pyrethrum was cut off by Japanese occupation of Southeast Asia and the Dutch East Indies (now Indonesia). Lead, arsenic, and copper compounds were needed for armaments and other military purposes. The British and Americans found themselves in need of an insecticide to protect soldiers from lice and ticks, the bearers of typhus. Those who had to fight in the jungles of the South Pacific needed protection from mosquitoes and other disease-bearing pests.

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*The common term *poison* is applied to a variety of substances, often without any indication of *degree* of toxicity. To avoid this uncertainty, biochemists use the term LD_{50} to indicate the dosage that would be lethal to 50% of a population of test animals. This dosage is expressed in amount of chemical per kilogram of body weight. The LD_{50} for human beings can usually only be estimated. What is toxic in rats may not be as toxic in humans. Or it might be more toxic. General trends in toxicity can usually be judged from animal studies. Toxicities of some insecticides are listed in **table 15.2.**

Table 15.2
Toxicity of some insecticidal preparations administered orally to rats

Pesticide	*LD_{50} (in milligrams of pesticide per kilogram of body weight)*
Pyrethrins*	1200
Lead arsenate	800
Carbaryl	540
DDT	113‡
Lindane	88
Nicotine sulfate†	55
Dieldrin	46
Methyl parathion	17
Endrin	8
Parathion	5

*Active ingredients of pyrethrum.
†Nicotine is much more toxic by injection.
‡Estimated LD_{50} for humans is 500 mg/kg.

The Allies obtained a few pounds of DDT* and hurriedly tested the compound. Combined with talcum, it made a very effective delousing powder. Clothing was impregnated with DDT. What is more, it seemed to have no deleterious effect on humans or other large animals. Allied soldiers were virtually free from lice, even though, in previous wars, more soldiers had probably died from typhus than from bullets. The Germans, as with the atomic bomb, missed out on DDT even though it was discovered "next door." Their troops were heavily infested with lice; many were sick with typhus.

The effectiveness of DDT was dramatically demonstrated in Naples shortly after allied troops captured the city. Bombing had destroyed two-thirds of the city, including the public waterworks. Virtually the only water available was from the sewers. Insects bred rapidly in the rubble, and there was a general lack of sanitation. A massive typhus epidemic broke out. The

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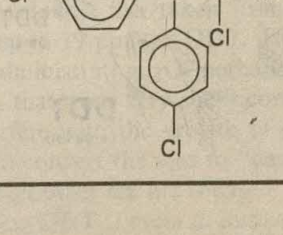
*DDT is an acronym for dichlorodiphenyltrichloroethane. Its structure is



people dusted themselves with DDT and liberally sprayed the chemical about. The epidemic was quickly brought under control.

In the Pacific, DDT was sprayed from planes to control malaria. Tents and branches were doused with it. The results were remarkable. DDT was one of several scientific developments which contributed greatly to the Allied cause. Healthy troops are more effective soldiers than sick ones.

The use of DDT increased rapidly in the years following World War II. In 1948, Müller was awarded the Nobel Prize in physiology and medicine for his discovery. Not only had DDT helped win the war for the Allies, but it seemed that the world would be free at last from insects and insect-borne diseases. Plant crops would be protected from the ravages of insects and food production increased. The millennium seemed at hand.

Fairly soon after the war there were a few warning rumbles (largely ignored) that all might not be rosy with DDT. In 1947, the magazine *Chemistry* devoted 24 pages to the praise of DDT, but it did include a warning to remove goldfish bowls and aquariums from a room before spraying. DDT was known to be highly toxic to tropical fish. Toxicity to other animals was noted but for the most part ignored. It was assumed that the toxicity would disappear soon after the chemical was discharged into the environment.

As early as 1946, houseflies resistant to DDT had been discovered. By 1948, 11 other DDT-resistant species had been noted, but use of the chemical continued at an ever-increasing rate. By 1962, the year that Rachel Carson's prophetic book *Silent Spring* was published, United States production of DDT had reached 76 000 000 kg (167 000 000 lb) per year.

For years Carson was roundly denounced by pesticide manufacturers and others. But by 1972, increasing problems with DDT led to Carson's (at least partial) vindication. (Unfortunately, that vindication came 8 years after her death from cancer.) It was in 1972 that the U.S. Environmental Protection Agency banned general use of DDT. Under certain conditions, it may still be used on three minor crops: green peppers, onions, and stored sweet potatoes. DDT may still be used to protect public health. For exam-

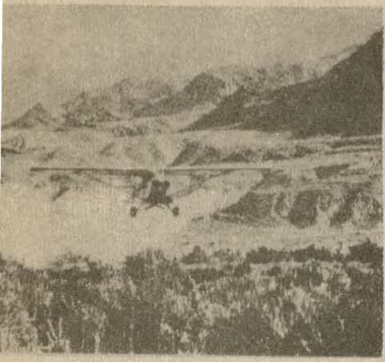


Figure 15.5 The first airplane to land on and take off from the shores of the Dead Sea (24 October 1955) was spraying insecticides against mosquitoes near Gora Sofi, Jordan, as part of a demonstration project sponsored by the U.S. Department of State in the Middle East, Asia, and Africa. The United States is the major supplier of DDT throughout the world. (Courtesy of the U.S. Department of Agriculture, Washington, D.C.)

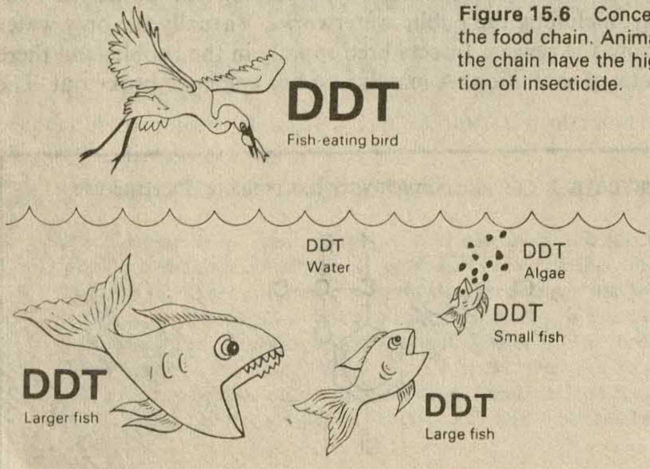


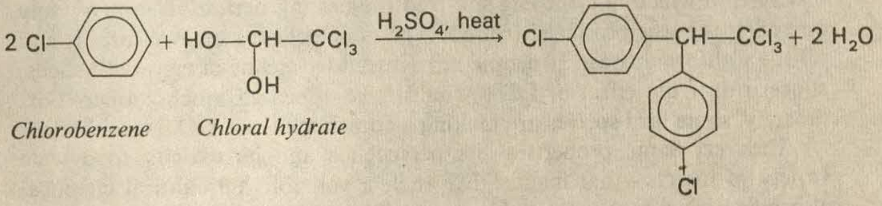
Figure 15.6 Concentration of DDT up the food chain. Animals at the top of the chain have the highest concentration of insecticide.

ple, in case of an outbreak of typhoid or malaria, DDT could be used to spray mosquito-infested areas. Production of DDT was not banned. It is still produced for export, particularly to developing countries, where it plays a major role in malaria control.

Before leaving the subject of DDT, let's look at its chemical and physical properties. A closer, longer look earlier in the history of the compound might have saved us all a lot of grief.

15.8 The Chemistry and Biochemistry of DDT

DDT is easily synthesized from cheap, readily available chemicals. Chlorobenzene and chloral hydrate are warmed in the presence of sulfuric acid.



Chlorobenzene *Chloral hydrate*

DDT

When the reaction is complete, the mixture is poured into water, and the DDT separates out, for, like other chlorinated hydrocarbons, DDT is essentially insoluble in water. Recall that the chlorinated hydrocarbons are good solvents for fats. But the reverse is also true: fats are good solvents for chlorinated hydrocarbons such as DDT. When DDT is ingested as a contaminant of food or water or when it is inhaled in air, it is extracted and concentrated by fatty tissues.

It is this fat-soluble nature of DDT that causes it to be concentrated up the food chain. This biological magnification was graphically demonstrated in California in 1957. Clear Lake, about a hundred miles north of San Francisco, was sprayed with DDT in an effort to control gnats. The water, after spraying, contained only 0.02 ppm of DDT. The microscopic plant and animal life contained 5 ppm—250 times as much. Fish feeding on these microorganisms contained up to 2000 ppm. Grebes, the diving birds that ate the fish, died by the hundreds.

Oysters and other shellfish concentrate DDT readily. Many formerly productive coastal areas are now completely devoid of these valuable food sources. Coho salmon, a valuable fish taken from Lake Michigan, were found in 1969 to contain up to 19 ppm of DDT. Their sale was prohibited by the Food and Drug Administration. Of perhaps greater importance in the long run is the finding that even very small concentrations of DDT (a few parts per billion) interfere with the growth of plankton in the ocean. An increased buildup could convert the seas to "deserts" devoid of all life, for it is plankton on which all other sea life is based.

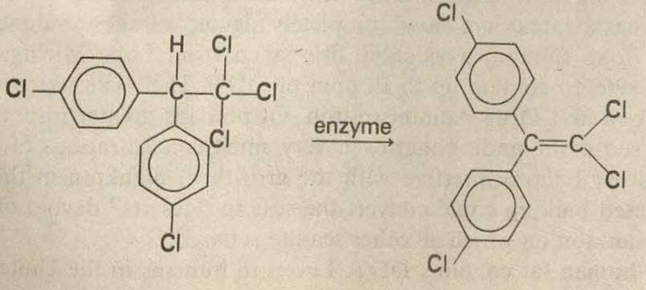
Even human fat contains DDT. Levels in humans in the United States declined from 8.0 ppm in 1971 to 5.9 ppm in 1973. If we were cannibals, human flesh still could not be sold, though, because of its high DDT content. Mother's milk would be banned for the same reason.

Biochemically, DDT is a nerve poison (chapter 20). DDT concentrates in phospholipids (chapter 23), compounds related to fats. Phospholipids are important constituents of brain and nerve tissue. DDT also interferes with calcium metabolism, essential to the formation of healthy bones and teeth. Although no harm to humans has ever been conclusively demonstrated, the disruption of calcium metabolism in birds has been disastrous for some species. Ingestion of DDT by some birds has resulted in their egg shells (which are composed mainly of calcium compounds) being thin and poorly formed. The bald eagle, our national symbol, is an endangered species. The peregrine falcon is near extinction. Whole colonies of these birds have been observed in which not one egg survived the nesting period unbroken. Only one offspring was produced from 552 pairs of pelicans on Anacapa Island off the California coast. If people reproduced by means of eggs with shells, concern over the effect of DDT would have appeared much sooner. Fortunately, some bird species are making a comeback since DDT was banned.

The very same properties—its persistence and its toxicity to a wide variety of insects—that made DDT such a valuable agricultural chemical also made it an environmental concern. Since DDT is sparingly soluble in water, it remains in nature for a very long time. It resists chemical decomposition, a property typical of chlorinated hydrocarbons. The pesticide has been found all over the world, even in Antarctica. Half a billion kilograms (more than a billion pounds) have been introduced into the biosphere. Some of the DDT sprayed from planes is carried into the upper atmosphere, to come down eventually in rainwater in even the most remote areas. And DDT kills beneficial insects, such as bees, as well as harmful ones.

15.9 The Insect Underground: Resistance to Pesticides

Insects often go through several generations in one summer. Genetic change through mutation can be very dramatic in only a few years. A genetic change in houseflies, enabling them to produce an enzyme catalyzing the detoxification of DDT, became apparent as early as 1946. The chemistry of that process has now been worked out. The enzyme brings about the removal of a hydrogen atom and a chlorine atom from DDT molecules to form a compound called DDE, which has been estimated to be about 150 times less toxic than DDT.



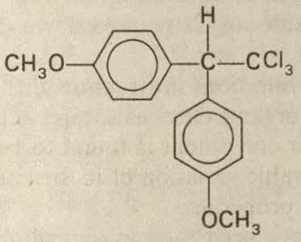
DDT *DDE*

Destruction of flies with DDT is now virtually impossible in most areas of the world. The resistant variants have survived and multiplied, while those without resistance have been killed off. Most fly populations are now largely made up of resistant strains.

Other insects have also developed resistant strains. In Korea, body lice (carriers of typhus) can no longer be controlled by DDT. Fleas (carriers of plague) have developed resistance in some areas. Mosquitoes (carriers of malaria and yellow fever) have developed immunity in much of the world. Heavy use of DDT has even resulted in an *increase* in insect pests where it has killed off their natural predators. The predator concentrates DDT by eating many insects which contain smaller amounts of the insecticide. This leads to interference with reproduction—or even death—in the predator.

15.10 Other Chlorinated Hydrocarbon Pesticides

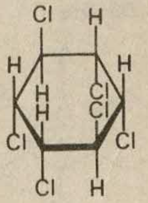
The early successes of DDT led to the search for other chlorinated hydrocarbon pesticides. Some, such as methoxychlor,



closely resemble DDT in structure and properties. Methoxychlor is significantly less toxic to mammals than DDT and seems to be broken down more readily in the environment.

Another type of chlorinated hydrocarbon pesticide is derived from benzene. Addition of chlorine to benzene in the presence of intense light of the proper wavelength gives a mixture of isomers collectively called benzene hexachlorides (BHC). (The structural formula shown at right indicates that BHC no longer contains an aromatic ring but is a chlorinated cyclohexane.)

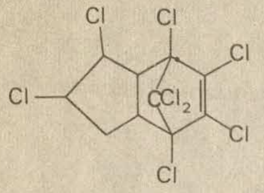
$$C_6H_6 + 3\,Cl_2 \xrightarrow{\text{light}} \underset{BHC}{C_6H_6Cl_6}$$



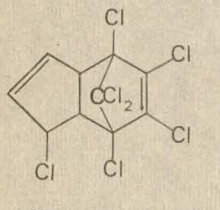
γ-Benzenehexachloride (lindane)

Lindane is the commercial name for one of the isomers isolated in essentially pure form. This isomer, called *gamma*-BHC, is also the only significant active ingredient in the BHC mixture. Structurally, the isomers differ in the arrangement of the chlorine atoms above and below the ring. The *gamma* isomer is shown here. Lindane has found wide use in many formulations, notably those for household use. BHC is used extensively in the control of cotton insects.

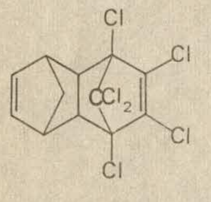
Perhaps the most important compounds that came out of the search for new chlorinated hydrocarbon pesticides are those containing several rings. Chlordane, heptachlor, endrin, aldrin, and dieldrin are examples.



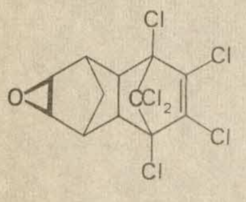
Chlordane



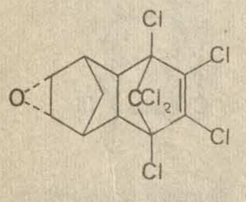
Heptachlor



Aldrin



Dieldrin



Endrin

Chlordane has been used extensively in agriculture, in gardens, and on lawns. Its structure is shown in the margin. (Recall that each corner in such a structure represents a carbon atom and enough hydrogen atoms to give the carbon four bonds.) Commercial chlordane contains two isomers of chlordane, some heptachlor, and other chlorinated products.

Heptachlor is a compound whose structure is closely related to chlordane. It has seven chlorine atoms (one fewer than chlordane) and two double bonds (one more than chlordane). Heptachlor is used against household pests, such as flies and mosquitoes. It is also used in agricultural formulations, often mixed with fertilizer for the control of pests in the soil.

Aldrin and dieldrin bear a strong resemblance to heptachlor and chlordane, and they are closely related to one another. Indeed, if aldrin is absorbed into the body, it is converted into dieldrin and stored in that form. The structure of aldrin is given in the margin. Dieldrin has a three-membered oxygen-containing ring (an epoxide) in place of one of the double bonds. Endrin is isomeric with dieldrin. The difference lies in the direction of the epoxide ring. In dieldrin, the oxygen is directed up (shown on the page by heavy lines). In endrin, the epoxide ring is pointed down (shown on the page by dotted lines).

The sometimes subtle variations in structure illustrated by this group of compounds are typical of organic chemicals, especially those of commercial importance. If a particular compound is found to be useful for some purpose, almost every conceivable variation of its structure will be synthesized and tested for comparable properties.

Dieldrin and aldrin have been used in agriculture and forestry, where long-lasting residual effect was considered advantageous. Dieldrin has also been used against ticks, chiggers, sand flies, and some species of mosquitoes. Endrin has been used on soil and foliage insects, with limitations set to prevent residues in food.

All these chlorinated hydrocarbons are toxic, but acute toxicities vary widely. For example, aldrin is about 150 times as toxic to rats as methoxychlor. Most of the chlorinated hydrocarbons seem to be especially toxic to fish. Massive fish kills (**figure 15.7**) have been caused by chlorinated hydrocarbon pesticides. The ghastly kill on the lower Mississippi River in 1963 was presumably caused by endrin, thought to have been dumped by a chemical plant in Memphis. Although the case against the company was never proven, close federal supervision of the plant brought a halt to the discharge of endrin. Once the discharge stopped, so did the fish kills.

In 1974, the Environmental Protection Agency set out to ban the manufacturing of aldrin and dieldrin after laboratory data linked these chemicals to cancer in mice and rats. Similar concern caused the EPA to move against chlordane and heptachlor in 1975. Low levels of these and other chlorinated hydrocarbons have been found in the municipal water supplies of a number of cities. The EPA concluded that continued use of these pesticides presented "an imminent hazard to human health."

As environmentalists have put pressure on one compound after another, an insecticide called toxaphene has increased in economic importance. Toxaphene is not a single compound but a mixture of products formed by the

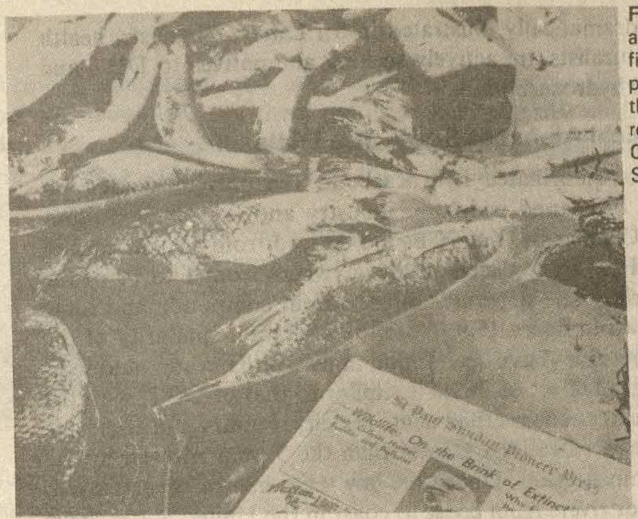
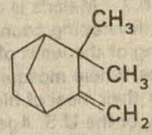

St Paul Sunday Pioneer Press
Wildlife: On the Brink of Extinction

Figure 15.7 In 1969, a loss of 41 million fish was attributed to pollution. (Courtesy of the Minnesota Environmental Control Citizens Association, St. Paul.)



Camphene

chlorination of camphene. Toxaphene molecules have an average of about eight chlorine atoms. Toxaphene is used against insects that attack cotton, forage crops, and some vegetables. But this insecticide, too, has caused problems. In streams, it has been shown to cause gross deformity of the spine in certain fish species.

15.11 Chlorinated Hydrocarbon Pesticides: The Balance Sheet

On the credit side of the balance sheet, DDT and other chlorinated hydrocarbons have (according to the World Health Organization) saved approximately 25 million lives and prevented hundreds of millions of illnesses. In India alone, malaria cases were reduced from 75 million to 5 million per year. The average life span in India has been increased 15 years since the mosquito-eradication program began in 1954.

Striking evidence of the value of DDT in public health comes from Sri Lanka (formerly Ceylon). There were 2.8 million cases of malaria in 1946. By 1963, spraying with DDT had reduced the incidence of malaria to only 17 cases. The spraying program was terminated in 1964. By 1968, the number of cases had risen to over 1 million per year.

On the debit side of the ledger, we have the near extinction of several species of birds, the massive fish kills, and the eradication of beneficial insects.

That nature can recover—at least from the amounts of DDT that have been used to date—is illustrated by the return of robins to the American Midwest. In the 1950s and 1960s, DDT was used extensively on crops and for the control of Dutch elm disease. Earthworms in the soil concentrated the DDT in their fatty tissue. Robins that ate the worms died by the thousands. Since DDT spraying was terminated in the 1960s, the robins have returned to former population levels.

The problem of a worldwide ban on DDT may solve itself as more and more insect species develop resistance. Its use may be discontinued simply because it is no longer effective. But the need for some type of insect control

Figure 15.8 Malaria is controlled in developing countries by spraying of the walls of the houses, where mosquitoes alight after their meal of blood. (Courtesy of the U.S. Agency for International Development, Washington, D.C.)

is apparent, as was dramatically illustrated in Sri Lanka. Chemists, health officials, and agriculturalists are actively seeking alternatives to DDT and the other chlorinated hydrocarbons.

15.12 More Chemical Alphabet Soup: The PCBs

Another group of chlorinated hydrocarbons, the polychlorinated biphenyls (PCBs), has been used widely in industry and is now ubiquitous in the environment. Chemically, the PCBs are derived from a hydrocarbon called biphenyl ($C_{12}H_{10}$) by replacement of anywhere from 1 to 10 of the hydrogens with chlorine. The structures of the parent compound and some of the PCBs are shown in **figure 15.9.** Note the structural similarity of the PCBs to DDT. PCB residues have been found in fish, birds, water, and sediments. The physiological effect of PCBs is similar to that of DDT, with the long-term effect of greater concern than acute toxicity. Poultry and eggs have been found to have concentrations greater than the 5 ppm allowed by the Food and Drug Administration. Under the law these had to be destroyed. Fish, taken from major rivers from coast to coast in the United States, have been found to be contaminated with PCBs, often above the 5-ppm maximum allowed by the Food and Drug Administration.

PCBs have found two main uses. Some plastics, particularly the vinyl types (chapter 21), are difficult to process. They can be made more flexible and easier to handle by addition of certain chemicals called plasticizers, which, ideally, are liquids of low volatility, such as the PCBs. These plasticizers are generally lost to the environment as the article containing them ages. Those used in auto seat covers sometimes show up on the car windows as a "fog" that is almost impossible to remove. Discarded plastics also release PCBs to the environment.

The other major use of PCBs is in electrical equipment. PCBs have a high electrical resistance, making them useful as insulating materials in trans-

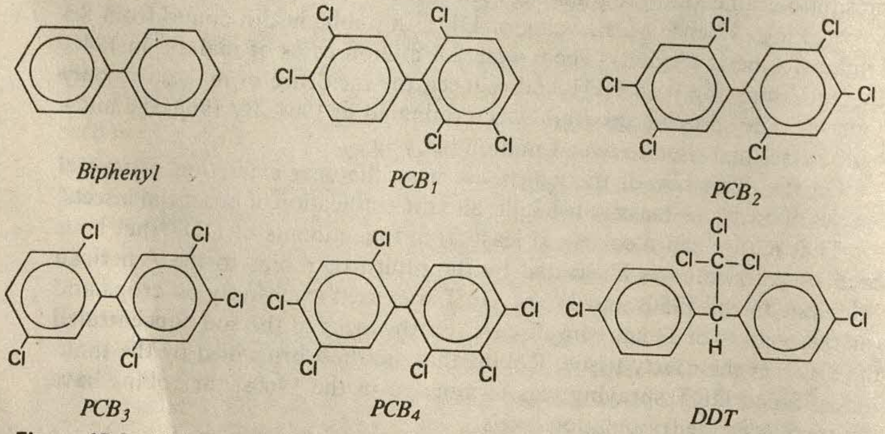


Figure 15.9 Biphenyl and some of the PCBs derived from it. Note that PCB$_1$ and PCB$_3$ are isomers with the formula $C_{12}H_5Cl_5$. These are but a few of the hundreds of possible PCBs. DDT is shown for comparison.

formers, condensers, and other electrical apparatus. They also have high boiling points, making them useful as heat transfer media. PCBs have a density greater than that of water (like many polyhalogenated hydrocarbons). Hence, when added to lubricants for underwater use, they increase the density of those lubricants.

The properties that made the PCBs so desirable as industrial chemicals—particularly their stability and solubility—cause them to be an environmental hazard. They degrade very slowly in nature, and their solubility in nonpolar media—animal fat as well as vinyl seat covers—leads to their concentration in the food chain. In humans, accidental ingestion has caused skin, liver, and gastrointestinal problems. Experiments with monkeys show that levels of less than 5 ppm in food interfere with reproduction.

Monsanto Corporation, the only company in the United States that produced PCBs, discontinued production in 1977, but PCBs will remain in the environment for years.

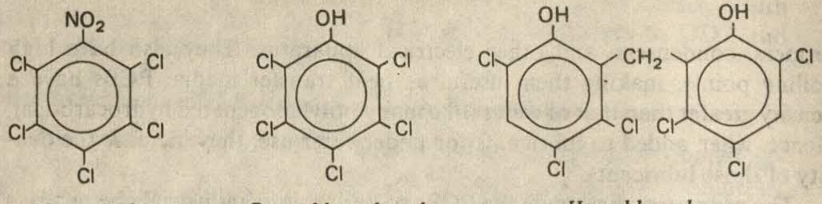
15.13 Polychlorinated Practically Everything

Pentachloronitrobenzene is used as an agricultural fungicide. Pentachlorophenol is a wood preservative, an algacide, and a fungicide. Hexachlorophene is a germicide, especially effective against staphylococcus infections. It has also caused neurological damage and even death in infants. 2,4-Dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) have been widely used as herbicides and defoliants. These last compounds were used extensively in Vietnam in an attempt to remove enemy cover and to destroy crops which maintained enemy armies. In addition to causing vast ecological damage, 2,4-D and 2,4,5-T were suspected of causing birth defects in Vietnamese children. Laboratory studies show that these compounds, when pure, do not cause abnormalities in fetuses of laboratory animals. Extensive birth defects are caused, though, by contaminants called dioxins, once frequently found in the herbicides. These dioxins are also chlorinated compounds.

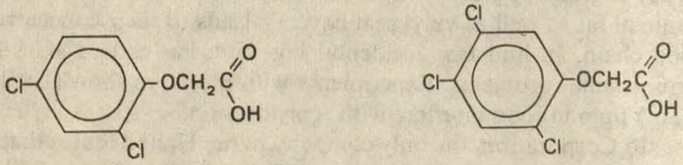
Structural representatives of these polychlorinated compounds are given in **figure 15.10.**

Late in 1974, still another problem with chlorinated compounds arose. Some 66 organic compounds were found in New Orleans drinking water. Among them were several chlorinated compounds. Chloroform, for example, was present at 0.1 ppm. Chlorinated phenols were also found. Some of the compounds, including chloroform, are suspected carcinogens.

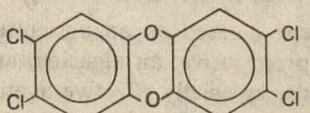
Most of the chlorinated compounds were probably formed by the reaction of organic wastes with the chlorine that is used to kill bacteria in the water. Even more frightening, people who drank New Orleans water (from the Mississippi River) had a 15% higher incidence of cancer than those who got their water from wells. The Environmental Protection Agency began a survey of water supplies in other cities. People became quite perturbed by the idea of getting cancer from drinking water. To put things somewhat in perspective, however, we might note that several popular cough medicines contained chloroform at a thousand times the concentration found in New



Pentachloronitrobenzene *Pentachlorophenol* *Hexachlorophene*



2,4-Dichlorophenoxyacetic acid *2,4,5-Trichlorophenoxyacetic acid*



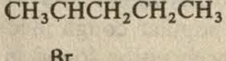
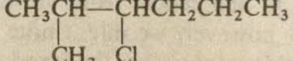
2,3,7,8-Tetrachlorodibenz-p-*dioxin*

Figure 15.10 Polychlorinated potpourri. There is the potential for good and bad in most of these compounds, depending on how they are used.

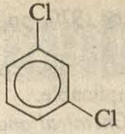
Orleans drinking water. Increasing concern over the physiological effects of chloroform, however, has led to the removal of chloroform from these formulations too.

Halogenated hydrocarbons were long regarded with lack of interest. Unlike the alcohols of the next chapter, they had no fascinating history or clearly perceived relation to life. We have tried to indicate in this chapter just how wrong that early judgment was.

Problems

1. What is meant by *aliphatic?* By *R?* By *aryl?* By *Ar?*
2. Write structures for the two isomers which have the molecular formula C_3H_7Br. Give the common name and the IUPAC name of each.
3. Write structures for the four isomers which have the molecular formula C_4H_9Cl. Give the common name and IUPAC name of each.
4. Draw structures for the following.
   - a. perfluoropropane
   - b. vinyl fluoride
   - c. carbon tetrachloride
   - d. chloroform
   - e. methylene chloride
   - f. 1,1-dichloropropylene
   - g. 2,4-dibromotoluene
5. Give the IUPAC name for each of the following.
   - a. 
     $CH_3\underset{Br}{CH}CH_2CH_2CH_3$
   - b. 
     $CH_3\underset{CH_3}{CH}-\underset{Cl}{CH}CH_2CH_2CH_3$

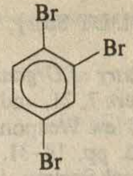
c.



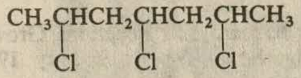
d. CH_3CHCl_2

e. $CHCl_2CH_2Cl$

f.



g.



$CH_3\underset{\underset{Cl}{|}}{C}HCH_2\underset{\underset{Cl}{|}}{C}HCH_2\underset{\underset{Cl}{|}}{C}HCH_3$

6. Compare halogenated hydrocarbons to hydrocarbons with respect to boiling point, density, and solubility.
7. As an anesthetic, what advantage did chloroform possess over ether? Why is chloroform no longer used as an anesthetic?
8. In general, what is the structure of the freons? In what types of products has their use been questioned?
9. Look up (use *The Merck Index* or a similar reference) the toxicities of the compounds shown in **figure 15.10**. Are these compounds poisons? Why or why not?
10. Examine the label of a household pesticide. List its trade name and its active ingredients. Look up the properties of the active ingredients.
11. What two properties of halogenated hydrocarbons, besides their toxicity, make these compounds useful as pesticides as well as dangerous in the environment?
12. What is the DDT level in humans at the present time? Is it likely to increase or decrease?
13. How much DDT would it take to kill a person weighing 60 kg (132 lb) if the lethal dose is 0.5 g per kilogram of body weight?
14. What is meant by the sentence "DDT is concentrated up the food chain"?
15. Name two animal classes (excluding insects) particularly susceptible to the lingering effects of pesticides in the environment.
16. Why is DDT no longer useful against some insect pests?
17. In early attempts to determine contaminants in biological systems, PCBs were often mistaken for DDT or other chlorinated hydrocarbon pesticides. Why might this be expected?
18. Name three pesticides besides DDT.

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chapter 16

Alcohols, Phenols, and Ethers

Unlike the halogenated hydrocarbons, the families of organic compounds discussed in this chapter occur naturally throughout the environment. And the human race has been quick to adapt these materials to its own use. The earliest written histories record the isolation and use by primitive peoples of the compound known as alcohol. According to Genesis, Noah planted a vineyard after the flood, drank wine from its grapes, and became drunk.

Human ingenuity may have reached some sort of peak in finding sources of *aqua vitae,* the water of life. Alcohol has been obtained from the fermentation of fruits, grains, potatoes, rice, and even cactus. It was prescribed as medicine in the 12th century but has been most frequently used without such justification. What we know as alcohol is actually only one member of a family known by the same name. The family includes among its members such familiar substances as cholesterol and the carbohydrates.

The name of another family of organic compounds considered in this chapter, the ethers, has become almost synonymous with anesthesia. And anyone who has ever been in a hospital would recognize the pungent, antiseptic odor of phenol, the simplest member of the third family to be introduced in this chapter.

Why are we taking up three different families in this one chapter? We do so because each can be considered an organic derivative of water. Water is by far the most important inorganic compound we have studied. It should not be surprising, therefore, that organic compounds derived from water are also of critical importance to life and health. Some, like the carbohydrates, deserve to and will be considered in a separate chapter (chapter 22). For now, we shall, as usual, deal with the simpler members of each family.

16.1 Where It's At: The Functional Group

Alcohols, phenols, and ethers can be viewed as organic derivatives of water. Consider the water molecule.

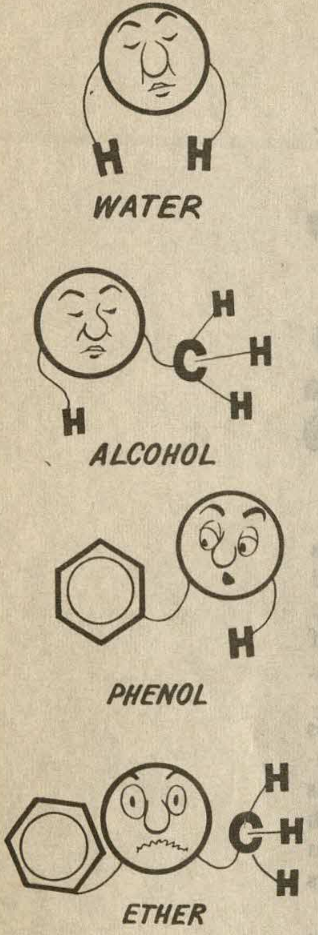
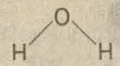
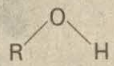


Figure 16.1 Alcohols, phenols, and ethers can be considered derivatives of water.

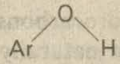


It is a bent molecule with the central oxygen attached to two hydrogen atoms. If one of these hydrogens were removed and replaced with an alkyl group (R—), we would have



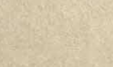
This is the general formula for the *alcohol* family. The alkyl group may be methyl, ethyl, *tert*-butyl, or an aliphatic group too complicated to have a simple name. As long as the carbon attached to the *hydroxyl group* (—OH) is aliphatic, the compound is an alcohol.

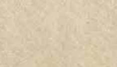
If the hydroxyl group is attached directly to an aromatic ring, a different family of compounds is produced. Compounds in which an aryl group (Ar—) is attached to a hydroxyl group are called *phenols.*

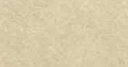


The chemistry of the phenols is sufficiently different from that of the alcohols to justify treatment of the two classes of compounds as separate, if closely related, families. Nonetheless, for both families, the chemistry is largely determined by the hydroxyl group. Nearly all the characteristic reactions of alcohols and many of those of the phenols take place at the hydroxyl group. Even the physical properties are determined to a large extent by the presence of the hydroxyl group. Such a group of atoms, which confers characteristic chemical and physical properties on a family of organic compounds, is called a *functional group*. The hydroxyl group is only one functional group We have already encountered others. The carbon-carbon double bond in alkenes and the carbon-carbon triple bond in alkynes are functional groups. In both instances, these structural features confer on the members of the families a particular chemical reactivity. For example, alkenes and alkynes tend to undergo addition reactions. The halogens in halogenated hydrocarbons are functional groups, although we did not consider in detail the particular reactions associated with these groups. The alkanes are characterized by their *lack* of a distinct functional group.

We have shown how both alcohols and phenols can be derived from a water molecule. We can also start with the water molecule and derive a general structure for a third family of organic compounds, the *ethers*. The ether family is the only one of the three which does not contain the hydroxyl functional group. To accomplish this, starting with a water molecule, we must substitute carbon groups for both of water's hydrogens. There are three possible ways of doing this.





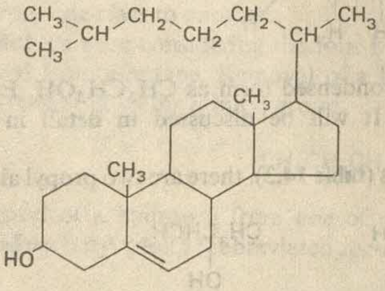


All of the above formulas represent ethers. A compound is an ether as long as there are two carbon groups attached to the oxygen, whether the groups are aliphatic or aromatic. No distinction is made in this case because no distinctive difference in chemical or physical properties is observed.

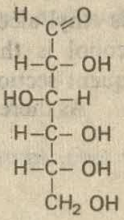
16.2 The Alcohols: Structures and Names

A compound containing a hydroxyl group attached to an aliphatic carbon atom is an alcohol. That takes in a lot of territory, as **figure 16.2** illustrates. The compounds pictured here are by no means among the largest alcohols known. The body stores complex alcohols (glycogen) for which formula weights in the millions have been recorded. The concept of a functional group, however, suggests that we can learn much about these complex molecules by studying simpler analogs.

The simplest alcohol has the formula CH_4O. When wood is heated in the absence of air until the wood breaks down and the vapors formed are collected, the alcohol with formula CH_4O is one of the products isolated



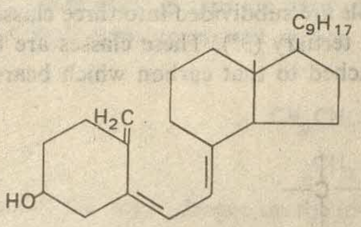
Cholesterol



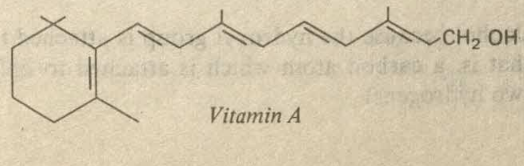
Glucose

$$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2OH$$

Tetracosanol



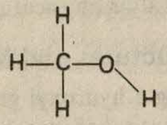
Vitamin D₂



Vitamin A

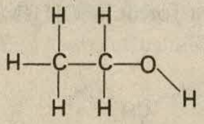
Figure 16.2 Some compounds containing the alcohol functional group. Cholesterol is found in all body tissues and is the main constituent of gallstones. Glucose is a simple sugar. Tetracosanol is an ingredient of beeswax. Vitamin D_2 is essential for proper formation of bones, and vitamin A is essential for good vision.

from the distillate. (This process is described as *destructive distillation.*) There is only one way to put together one carbon, four hydrogens, and one oxygen and not violate the rules of molecular architecture.



Notice that the compound can be thought of as a methyl group (CH_3—) joined to a hydroxyl group (—OH). In condensed form, the formula would be written as CH_3OH.

For simple alcohols, common names are often used. One merely names the alkyl group and then adds the word *alcohol* to indicate the presence of the hydroxyl group. Thus, CH_3OH is methyl alcohol. The compound

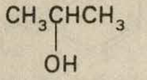


is ethyl alcohol. It is written in condensed form as CH_3CH_2OH. Ethyl alcohol is the beverage alcohol. It will be discussed in detail in subsequent sections.

As there are two propyl groups (**table 14.3**), there are two propyl alcohols.

$CH_3CH_2CH_2OH$

n-*Propyl alcohol*

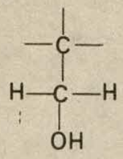


$$CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_3$$

Isopropyl alcohol

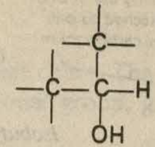
Isopropyl alcohol, in 70% and 91% solutions, is used as a topical antiseptic and in body rubs, after-shave lotions, and similar preparations.

The names of the butyl groups were first introduced in **table 14.3.** The present discussion of alcohols offers us an opportunity to explain where two of those names originated. Alcohols are subdivided into three classes, called primary (1°), secondary (2°), and tertiary (3°). These classes are based on the number of carbon atoms attached to that carbon which bears the hydroxyl group. The structure

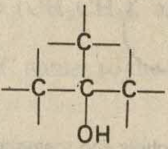


is classified as a primary alcohol because the hydroxyl group is attached to a primary carbon atom, that is, a carbon atom which is attached to only one other carbon (and to two hydrogens)

The alcohol



is secondary, because the hydroxyl group is attached to a secondary carbon, one which is bonding to two other carbons (and to one hydrogen). Finally, if the hydroxyl group is attached to a carbon bonded to three other carbon atoms, the alcohol is called tertiary.

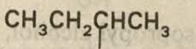


Some of the reactions of the alcohols, notably oxidation (section 16.6), differ from one class to another.

But we were considering the four butyl alcohols. Two butyl groups are derived from *n*-butane. Removal of a hydrogen atom from an end carbon on *n*-butane gives the *n*-butyl group.

$$CH_3CH_2CH_2CH_2—$$

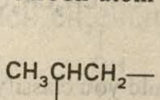
Removal of a hydrogen from one of the interior carbon atoms gives the *secondary* butyl group (abbreviated *sec*-butyl).



$$CH_3CH_2\underset{|}{C}HCH_3$$

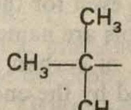
It is now easy to see why this group is called secondary butyl; the attachment of this butyl group to a longer chain or to a functional group, such as a hydroxyl group, is made through a carbon atom which is attached to two other carbon atoms, that is, through a secondary carbon atom.

Two other butyl groups are derived from isobutane. Removal of any of the nine hydrogens on an end carbon atom of isobutane gives an isobutyl group.

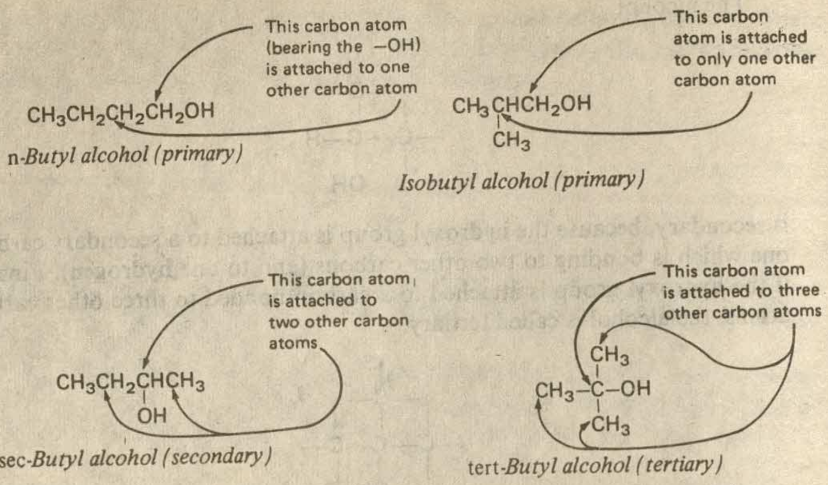


$$CH_3\underset{\underset{CH_3}{|}}{C}HCH_2—$$

Removal of the one hydrogen on the interior carbon atom gives the *tertiary* butyl group (*tert*-butyl).



$$CH_3—\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}—$$


This carbon atom (bearing the –OH) is attached to one other carbon atom
CH3CH2CH2CH2OH
This carbon atom is attached to only one other carbon atom
CH3CHCH2OH
CH3
This carbon atom is attached to two other carbon atoms
CH3CH2CHCH3
OH
This carbon atom is attached to three other carbon atoms
CH3
CH3–C–OH
CH3

n-*Butyl alcohol (primary)*

Isobutyl alcohol (primary)

sec-*Butyl alcohol (secondary)*

tert-*Butyl alcohol (tertiary)*

Figure 16.3 The four butyl alcohols and their classification as primary, secondary, and tertiary.

Here the name reflects the fact that the attachment is made through a tertiary carbon atom, that is, one which is attached to three other carbon atoms.

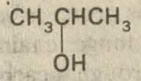
The four butyl alcohols are shown in **figure 16.3.**

Example 16.1 Classify each of the following alcohols as primary, secondary, or tertiary: ethyl alcohol, isopropyl alcohol, *n*-propyl alcohol.

Ethyl alcohol,

$$CH_3CH_2OH$$

is a primary alcohol. Isopropyl alcohol,



$$CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_3$$

is a secondary alcohol. *n*-Propyl alcohol,

$$CH_3CH_2CH_2OH$$

is a primary alcohol.

Example 16.2 How would you classify methyl alcohol?

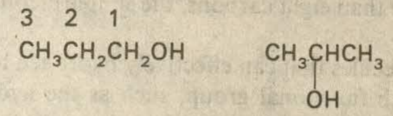
Methyl alcohol can't be classified under this system. There is only one carbon atom in methyl alcohol; therefore, it is attached to no other carbon atoms and is neither primary, secondary, nor tertiary.

More complex alcohols are generally given IUPAC names. These systematic names are often used even for the simplest members of the family. By the IUPAC system, alcohols are named for the alkane corresponding to the longest continuous chain of carbon atoms. The final *-e* of the alkane name is dropped and replaced by the ending *-ol.* If necessary, the position of the hydroxyl group is indicated by a number placed immediately in front of the name of the longest, parent chain. The molecule is always numbered from the end nearer the functional group, giving the hydroxyl group the lowest possible number.

Example 16.3 Give the IUPAC names for methyl alcohol and ethyl alcohol.

Methyl alcohol (CH_3OH) is named as a derivative of methane (CH_4). Merely drop the *-e*, add *-ol*, and you have it—methanol. To name CH_3CH_2OH, drop the final *-e* from the name of the corresponding alkane, ethane (CH_3CH_3), and add *-ol*. The IUPAC name is ethanol.

Example 16.4 Give IUPAC names to the two propyl alcohols.

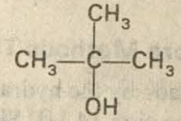


$$\overset{3}{C}H_3\overset{2}{C}H_2\overset{1}{C}H_2OH \qquad CH_3\underset{\underset{\displaystyle OH}{|}}{C}HCH_3$$

The names are, respectively, 1-propanol (not 3-propanol) and 2-propanol.

Example 16.5 Give the IUPAC name for *tert*-butyl alcohol.

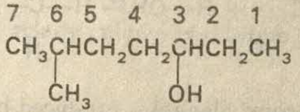
tert-Butyl alcohol is



$$CH_3-\underset{\underset{\displaystyle OH}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{C}}-CH_3$$

The longest continuous chain is three carbon atoms long, and the hydroxyl group is on the second carbon of this chain, yielding, for the moment, 2-propanol. There is also a methyl group hanging from the second carbon of the parent chain, giving 2-methyl-2-propanol.

Example 16.6 Give the IUPAC name for



$$\overset{7}{C}H_3\underset{\underset{\displaystyle CH_3}{|}}{\overset{6}{C}}H\overset{5}{C}H_2\overset{4}{C}H_2\underset{\underset{\displaystyle OH}{|}}{\overset{3}{C}}H\overset{2}{C}H_2\overset{1}{C}H_3$$

The name is 6-methyl-3-heptanol (*not* 2-methyl-5-heptanol).

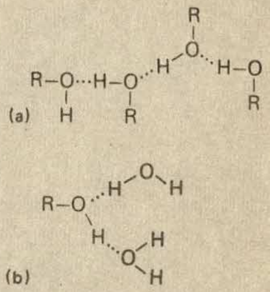


Figure 16.4 (a) Alcohols have high boiling points relative to the hydrocarbons because of strong intermolecular hydrogen bonding. (b) Alcohols of low molecular weight are soluble in water because the molecules can hydrogen bond to water molecules.

16.3 Physical Properties of the Alcohols

Most of the common alcohols are liquids at room temperature. The simplest one, methanol, boils at 65 °C. The hydrocarbon ethane, which has nearly the same molecular weight as methanol, boils at −89 °C and is a gas at room temperature. Here we see the pronounced effect of hydrogen bonding (section 7.3) on boiling points. **Figure 16.4a** shows how alcohol molecules may be associated through hydrogen bonding. Such association is less extensive in alcohols than in water (compare **figure 7.4**), because an alkyl group (R—) has replaced one of the hydrogen atoms. No hydrogen bond can occur through that alkyl group. Because of this, methanol has a lower boiling point than water even though the molecular weight of methanol is about twice that of water.

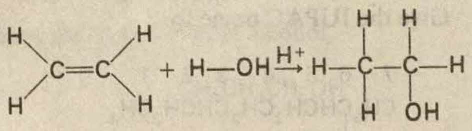
Alcohols of low molecular weight are soluble in water. Indeed, methyl, ethyl, and the two propyl alcohols can be mixed with water in all proportions; that is, they are completely miscible with water. As the size of the alkyl group increases, however, the alcohols become more like alkanes (they become more insoluble in water) and less like water itself. *n*-Octyl alcohol ($CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2OH$) is soluble only to the extent of 0.05 g in 100 g of water. The hydroxyl group's ability to form hydrogen bonds is almost totally overshadowed by the lack of attraction between water molecules and the long alkanelike hydrocarbon portion of the organic compound. With more than eight carbons, the simple alcohols are essentially insoluble in water.

To generalize, molecules that can effectively hydrogen bond to water will dissolve in water. Each functional group, such as the hydroxyl, which can form hydrogen bonds to water can carry along into solution an alkyl group of up to four or five carbon atoms. Thus, we will frequently find that the borderline of water solubility in a family of organic compounds occurs at four or five carbon atoms (**table 16.1**). For isomeric alcohols, the more branched structures lead to greater solubility (consider the four butyl alcohols).

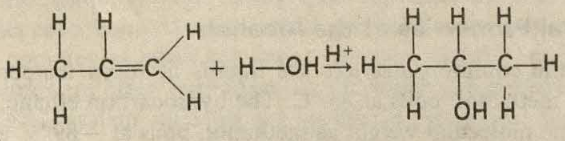
16.4 Making Alcohols: More Methods Than Moonshining

Most simple alcohols are made by the hydration of alkenes (the addition of water to the double bond—section 14.11). Since alkenes are made by the cracking of petroleum, our supply of most alcohols is dependent to a large extent on the availability of oil.

Ethyl alcohol is made by the hydration of ethylene in the presence of a mineral acid.



In a similar manner, isopropyl alcohol is produced by the addition of water to propylene.



With isobutylene, the product is *tert*-butyl alcohol.

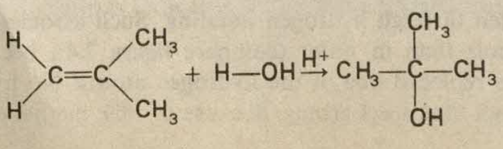
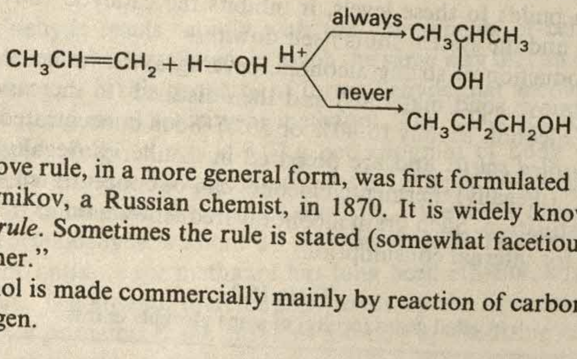


Table 16.1
Physical properties of some common alcohols

Name	*Formula*	*Boiling Point (in degrees Celsius)*	*Solubility (in grams per 100 g of water)*
Methyl alcohol	CH_3OH	64	∞
Ethyl alcohol	CH_3CH_2OH	78	∞
n-Propyl alcohol	$CH_3CH_2CH_2OH$	97	∞
n-Butyl alcohol	$CH_3CH_2CH_2CH_2OH$	118	7.9
n-Pentyl alcohol	$CH_3(CH_2)_3CH_2OH$	138	2.3
n-Hexyl alcohol	$CH_3(CH_2)_4CH_2OH$	156	0.6
n-Octyl alcohol	$CH_3(CH_2)_6CH_2OH$	195	0.05
n-Decyl alcohol	$CH_3(CH_2)_8CH_2OH$	228	(Insoluble)
Isopropyl alcohol	$CH_3CHOHCH_3$	82	∞
Isobutyl alcohol	$(CH_3)_2CHCH_2OH$	108	10.2
sec-Butyl alcohol	$CH_3CHOHCH_2CH_3$	99	12.5
tert-Butyl alcohol	$(CH_3)_3COH$	83	∞

Note that in the last two reactions, the hydrogen goes on the carbon atom (of the two involved in the double bond) that has the most hydrogens already bonded to it. The hydroxyl group goes on the carbon with fewer hydrogens. Thus, addition of water to propylene always gives isopropyl alcohol, never *n*-propyl alchol.



$$CH_3CH{=}CH_2 + H{-}OH \xrightarrow{H^+} \begin{cases} \xrightarrow{\text{always}} CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_3 \\ \xrightarrow{\text{never}} CH_3CH_2CH_2OH \end{cases}$$

The above rule, in a more general form, was first formulated by Vladimir V. Markovnikov, a Russian chemist, in 1870. It is widely known as *Markovnikov's rule*. Sometimes the rule is stated (somewhat facetiously) as "the rich get richer."

Methanol is made commercially mainly by reaction of carbon monoxide with hydrogen.

$$CO + 2\,H_2 \longrightarrow CH_3OH$$

The reaction is carried out at a high temperature and pressure and in the presence of a catalyst. Unlike the hydration reaction, this industrial process does not represent a general approach to the synthesis of a variety of alcohols.

Although of considerably less (but still great) economic importance, the process of making alcohol by fermentation may be of greater interest to many people. Most alcoholic beverages are made by fermentation of starches or sugars. On an industrial scale, either molasses from sugarcane or starches from various types of grain are fermented by yeast to ethyl alcohol. It is ethyl alcohol that most people are referring to when they say "alcohol," meaning liquor or that which is imbibed.

In the preparation of ethyl alcohol from grain, the seeds are ground and

Figure 16.5 Alcohol can be made by the fermentation of nearly any type of starchy or sugary material.

cooked, producing *mash*. Malt (the dried sprouts of barley) or a mold such as *Aspergillus oryzae* is added as a source of the enzyme *diastase*. This enzyme catalyzes the conversion of starch to malt sugar, *maltose*.

$$\underset{\textit{Starch}}{(C_6H_{10}O_5)_{2x}} + x\,H_2O \xrightarrow{\text{diastase}} \underset{\textit{Maltose}}{x\,C_{12}H_{22}O_{11}}$$

The maltose solution is diluted to 10% concentration and a pure yeast culture is added. The yeast cells produce two enzymes which catalyze the remainder of the fermentation process. First, the enzyme *maltase* converts the maltose to glucose.

$$\underset{\textit{Maltose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{\text{maltase}} \underset{\textit{Glucose}}{2\,C_6H_{12}O_6}$$

Then the enzyme *zymase* converts glucose to ethyl alcohol and carbon dioxide.

$$C_6H_{12}O_6 \xrightarrow{\text{zymase}} 2\,CH_3CH_2OH + 2\,CO_2$$

In the production of beer or malt liquor, part of the carbon dioxide is retained, making a carbonated beverage. The fermentation process is capable of yielding aqueous solutions containing up to 18% alcohol. As the alcohol concentration builds to these levels, it inhibits the catalytic activity of the yeast cultures and the system shuts itself down.

In the production of strong alcoholic beverages, the fermented mash is filtered (to remove solid materials) and then distilled (to increase the concentration of alcohol, usually to 40% or 50%). Such concentrated solutions are called *distilled spirits* and are prepared in distilleries (legally) or backwoods "stills" (illegally). Fermented alcohol can be concentrated to as much as 95% by distillation. Such grain alcohol is frequently used as a solvent for drugs meant for internal consumption.

Table 16.2
Lethal doses (orally) of some alcohols in rats

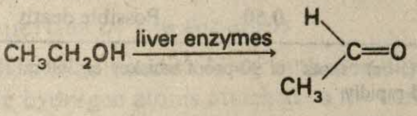
Alcohol	*Structure*	*LD_{50} (in grams per kilogram of body weight)*
Methanol	CH_3OH	
Ethanol	CH_3CH_2OH	13.7
1-Propanol	$CH_3CH_2CH_2OH$	1.87
2-Propanol	$CH_3CHOHCH_3$	5.8
1-Butanol	$CH_3CH_2CH_2CH_2OH$	4.36
1-Hexanol	$CH_3(CH_2)_4CH_2OH$	4.9
Ethylene glycol	$HOCH_2CH_2OH$	8.54
Glycerol	$HOCH_2CHOHCH_2OH$	31.5

Data from Windholz, Martha, ed., *The Merck Index*, 9th ed., Rahway, N.J.: Merck, 1976.

16.5 Alcohols and People: Physiological Properties

The simple alcohols are generally toxic to some degree, as **table 16.2** indicates. Note that no LD_{50} is given for methanol (wood alcohol). While its acute (short-term) toxicity is not terribly high, it can cause permanent blindness or death, even in small concentrations. Each year many accidents are attributed to this alcohol, which is frequently mistaken for its less harmful relative ethyl alcohol.

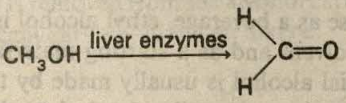
The reason methanol is so dangerous* is that humans and other primates have liver enzymes that oxidize primary alcohols to compounds called aldehydes. Ethanol, for example, is oxidized to acetaldehyde.



Ethanol *Acetaldehyde*

The acetaldehyde is in turn oxidized to acetic acid, a normal constituent of cells. The acetic acid can then be oxidized to carbon dioxide and water.

Similarly, methanol is oxidized to formaldehyde.



Methanol *Formaldehyde*

Formaldehyde reacts rapidly with the components of cells. It causes the protoplasm to be coagulated, in much the same way that an egg is coagulated by cooking. It is this property of formaldehyde that accounts for the great chronic (long-term) toxicity of methanol. The LD_{50} for formaldehyde administered orally to rats is 0.07 g per kilogram of body weight. That for acetaldehyde under the same conditions is 1.9 g per kilogram of body weight. (Keep in mind that, the *smaller* the LD_{50}, the *more toxic* the substance.) Thus, formaldehyde is about 27 times as toxic to rats as acetaldehyde. Indeed, the antidote for methanol has long been ethanol, administered intravenously. The ethanol preferentially loads up the liver enzymes in humans and other primates. If the enzymes are tied up oxidizing ethanol to acetaldehyde, they cannot catalyze the oxidation of the methanol to the dangerously toxic formaldehyde. Thus, the unoxidized methanol is gradually excreted from the body.

Despite its toxicity, methanol is a valuable industrial solvent. It is also a raw material for the production of other chemicals.

*It should be noted that methanol is not particularly toxic to horses, rats, and some other animals. These animals are lacking in the enzymes that oxidize alcohols to aldehydes. These facts should make it abundantly clear that toxicity studies in other animals cannot always be extrapolated to humans.

Table 16.3
Relationship between drinks consumed, blood alcohol level, and behavior. The data would be approximate for a 70-kg (154-lb) person who is a moderate drinker

*Quantity of Beverage**	*Blood-Alcohol Level (percent by volume)*	*Behavior*
2 "shots" or 2 beers	0.05	Mild sedation; tranquility
4 "shots" or 4 beers	0.10	Lack of coordination
6 "shots" or 6 beers	0.15	Obvious intoxication
10 "shots"	0.30	Unconsciousness
20 "shots"	0.50	Possible death

***Based on 30-ml (1-oz) "shots" of 90-proof whiskey or 360-ml (12-oz) bottles of beer, consumed rapidly.**

But ethanol (ethyl alcohol) is toxic, too. A pint of pure ethyl alcohol, rapidly ingested, would kill most people. Even the strongest alcoholic beverages, however, are seldom more than 90 proof (45%).* Excessive ingestion over a long period of time leads to deterioration of the liver and loss of memory—and possibly to strong physiological addiction.

In addition to its use as a beverage, ethyl alcohol is used in great quantities as an industrial solvent and as a starting material for other chemical products. Such industrial alcohol is usually made by the addition of water to ethylene. The product is structurally identical to the ethyl alcohol produced through fermentation. Alcoholic beverages are generally highly taxed. To avoid the diversion of untaxed industrial alcohol to use in beverages, the industrial alcohol is *denatured* by addition of other chemicals that make the alcohol unfit to drink. Among the common denaturants are gasoline and methanol. When necessary for laboratory work, pure ethanol is available for use. In the United States, this untaxed alcohol is strictly controlled by the federal government. Thus, in 1975, a chemist could buy for $1 an amount of alcohol equivalent to what would have cost about $15 in a liquor store. The price difference is due almost entirely to the taxes which you must pay for a product which is considered a luxury.

Ethyl alcohol acts as a mild hypnotic (sleep inducer). Perhaps this is fortunate, for a heavy drinker usually "passes out" before ingesting a lethal dose. Although it generally acts as a depressant (i.e., it reduces the level of consciousness and the intensity of our reactions to environmental stimuli), ethyl alcohol in small amounts seems sometimes to act as a stimulant. Any

---

***The "proof" is merely twice the percentage of alcohol by volume. The term has its origin in an old 17th-century method for testing whiskey. Dealers were perhaps too often tempted to increase profits by adding water to the booze. A qualitative method for testing the whiskey was to pour some of it on gunpowder and ignite it. If the gunpowder ignited after the alcohol had burned away, that was considered "proof" that the whiskey did not contain too much water.**

such effect, however, is probably due to the alcohol's action in relaxing tensions and relieving inhibitions.

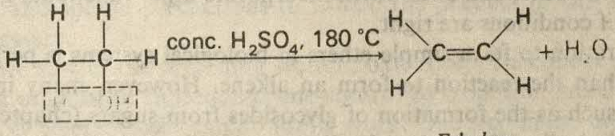
Isopropyl alcohol, an ingredient in rubbing alcohol and other products for external use, is sometimes mistaken for ethanol and is ingested. Though more toxic than ethanol, it seldom causes fatalities. Instead, it induces vomiting. It doesn't stay down long enough to kill you (though perhaps it stays down long enough to make you wish you were dead). Other higher alcohols behave in a similar manner.

The lower alcohols have a mild antiseptic action. Ethanol or isopropyl alcohol are often used to clean the skin before an injection, the drawing of blood, or minor surgery.

16.6 Chemical Properties of the Alcohols

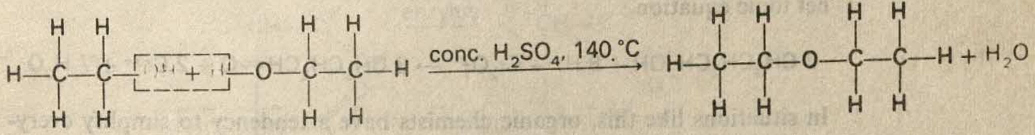
The reactions of the alcohols occur mainly at the functional group. They may, however, involve hydrogen atoms attached to the carbon bearing the hydroxyl group or even those on an adjacent carbon. We will discuss three major kinds of reactions of the alcohols. Dehydration and oxidation will be considered here. Esterification will be covered in chapter 18.

Dehydration (removal of water) is usually accomplished by addition of concentrated sulfuric acid to the alcohol and heating of the resulting mixture. The hydroxyl group is removed from the alcohol carbon and a hydrogen is removed from an adjacent carbon, giving an alkene.



Ethyl alcohol *Ethylene*

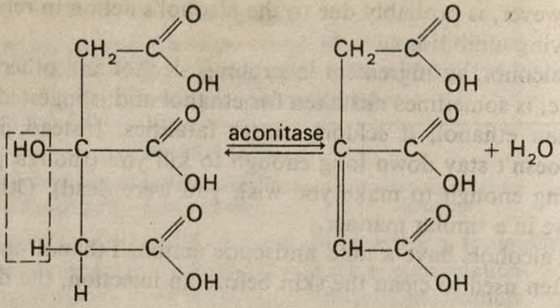
Under the proper conditions it is possible to carry out a dehydration involving two molecules of alcohol. In this case, the hydroxyl group of one alcohol is removed and only the hydrogen of the hydroxyl group of the second alcohol molecule is removed. The two organic groups remaining combine to form an ether molecule.



Two molecules of ethanol *Ethyl ether*

Thus, depending upon conditions, one can prepare either alkenes or ethers by dehydration of alcohols. At 180 °C, dehydration of ethanol gives ethylene as the main product. At 140 °C, the main product of dehydration of ethanol is ethyl ether.

Dehydration reactions also take place in biological systems. For example, in carbohydrate metabolism (chapter 30), citric acid is dehydrated to *cis*-aconitic acid.



Citric acid cis-*Aconitic acid*

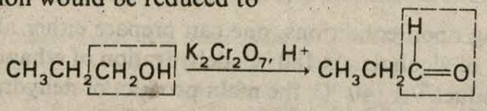
Look carefully at this equation. The compounds involved are more complex than the ethyl alcohol and ethylene we used in our previous example, but the reaction is not. Ignore all that stuff hanging off to the right of the molecules. These parts of the starting material remain unchanged (in this reaction) in the product. The only thing that has happened is that a hydrogen and a hydroxyl group have been eliminated from the starting material, and the product contains a double bond. The point to be made is that, if you know the chemistry of a particular functional group, you know the chemistry of a thousand or a hundred thousand different individual compounds. Alcohols have a potential for undergoing dehydration, and you will find that big ones, little ones, and ones which incorporate other functional groups all dehydrate if conditions are right.

Dehydration to form simple ethers in biological systems is perhaps less common than the reaction to form an alkene. However, many important reactions, such as the formation of glycosides from sugars (chapter 22) are at least technically dehydrations leading to etherlike compounds.

Primary and secondary alcohols are readily oxidized. In the preceding section we saw how methanol and ethanol are oxidized by liver enzymes to form aldehydes. Such reactions can also be carried out in the laboratory with chemical oxidizing agents. For example, in acid solution potassium dichromate oxidizes *n*-propyl alcohol to propionaldehyde. The balanced equation for this reaction is quite complicated, even if we write only the net ionic equation.

$$3\ CH_3CH_2CH_2OH + 8\ H^+ + Cr_2O_7^{2-} \longrightarrow 3\ CH_3CH_2CH{=}O + 2\ Cr^{3+} + 7\ H_2O$$

In situations like this, organic chemists have a tendency to simplify everything until only the change involving the organic molecules is shown. Thus, the above reaction would be reduced to



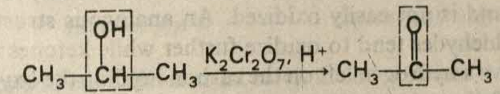
$$CH_3CH_2CH_2OH \xrightarrow{K_2Cr_2O_7,\ H^+} CH_3CH_2\overset{H}{\overset{|}{C}}{=}O$$

n-*Propyl alcohol* *Propionaldehyde*

The required inorganic reagents are written above the arrow (a place reserved for catalysts by inorganic chemists). The inorganic by-products are ignored (they're still formed, but we just ignore them in this form of the equation). In this way, all attention is focused on the organic starting material and product, and less time is spent balancing the frequently complicated equations.

The abbreviated form of this particular equation indicates that a primary alcohol is oxidized to an aldehyde. We shall see, in the next chapter, that aldehydes are even more easily oxidized than alcohols and yield as products carboxylic acids. If one wishes to isolate the aldehyde initially formed in the oxidation of the alcohol, it is necessary to remove it from contact with the oxidizing agent. This can be done by distillation of the aldehyde from the reaction mixture as it forms.

Secondary alcohols are oxidized to compounds called ketones. Oxidation of isopropyl alcohol by dichromate gives acetone.

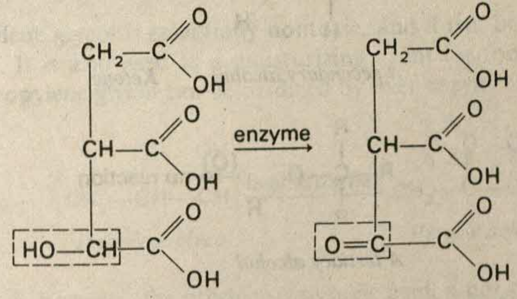


Isopropyl alcohol (a secondary alcohol)

Acetone (a ketone)

Unlike aldehydes, ketones are relatively resistant to further oxidation (chapter 17), and special precautions to isolate the product of this reaction are not necessary.

As we saw in the preceding section, oxidation of alcohols is important in living organisms. Indeed, enzyme-controlled oxidation reactions provide the energy whereby cells can do useful work. One step in the metabolism of carbohydrates (chapter 30) involves the oxidation of the secondary alcohol group in isocitric acid to a ketone group.

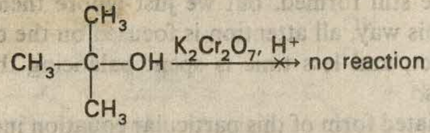


Isocitric acid

Oxalosuccinic acid

Again note that the overall reaction is identical to that of the conversion of isopropyl alcohol to acetone. The complications of structure which distinguish isocitric acid in no way interfere with the characteristic reaction of its secondary alcohol group.

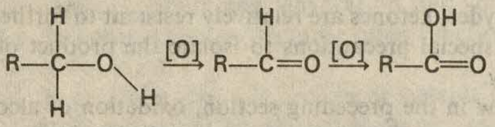
Tertiary alcohols are resistant to oxidation. Ordinary oxidizing agents, such as dichromate, bring about no change in this class of alcohols, which lacks a hydrogen on the carbon atom bonded to the hydroxyl group.



$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-OH \xrightarrow{K_2Cr_2O_7,\ H^+} \text{no reaction}$$

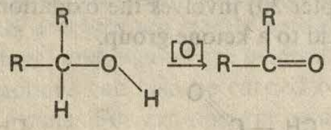
tert-*Butyl alcohol*

The oxidation reactions we have described involve the formation of a carbon-oxygen double bond. Thus, the carbon atom bonded to the oxygen in the alcohol must be able to release one of the atoms attached to it so it can form the double bond with oxygen. Hydrogen is particularly willing to leave the carbon under the conditions of oxidation. Both primary and secondary alcohols have a hydrogen on the carbon holding the hydroxyl group, and both these classes of alcohols are readily oxidized. The tertiary alcohol lacks such a hydrogen and is not easily oxidized. An analogous structural feature explains why aldehydes tend to oxidize further while ketones don't. The aldehydes still have a hydrogen left on the carbon holding the oxygen; the ketones do not. The following equations summarize the differences in the oxidation (indicated by the symbol [O]) of the various classes of alcohols.



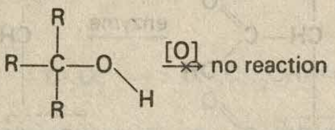
$$R-\overset{H}{\underset{H}{C}}-O-H \xrightarrow{[O]} R-\overset{H}{C}=O \xrightarrow{[O]} R-\overset{OH}{C}=O$$

A primary alcohol *Aldehyde* *Carboxylic acid*



$$R-\overset{R}{\underset{H}{C}}-O-H \xrightarrow{[O]} R-\overset{R}{C}=O$$

A secondary alcohol *Ketone*



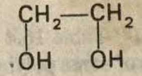
$$R-\overset{R}{\underset{R}{C}}-O-H \xrightarrow{[O]} \text{no reaction}$$

A tertiary alcohol

16.7 Multifunctional Alcohols: Glycols and Glycerol

The simple alcohols that we have met so far contain only one hydroxyl group each. They are called *monohydric* alcohols. Several important compounds that are frequently encountered contain more than one hydroxyl group per molecule. They are called *polyhydric* alcohols. Those with two such groups are said to be *dihydric*. Substances with three hydroxyl groups are called *trihydric* alcohols.

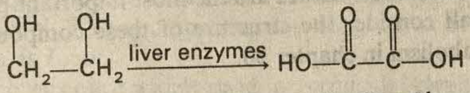
Dihydric alcohols are often called *glycols*. The most important of these is ethylene glycol.



$$\underset{\mathrm{OH}}{\mathrm{CH_2}}-\underset{\mathrm{OH}}{\mathrm{CH_2}}$$

This compound is the main ingredient in permanent antifreeze mixtures for automobile radiators. Ethylene glycol is a sweet, somewhat viscous liquid. With two hydroxyl groups, there is extensive intermolecular hydrogen bonding. Thus, ethylene glycol has a high boiling point and does not boil away when used as antifreeze. It is also completely miscible with water.

Ethylene glycol is quite toxic. As with methanol, its toxicity is due to a metabolite. Liver enzymes oxidize the ethylene glycol to oxalic acid.

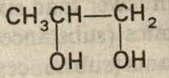


$$\overset{\mathrm{OH}}{\mathrm{CH_2}}-\overset{\mathrm{OH}}{\mathrm{CH_2}} \xrightarrow{\text{liver enzymes}} \mathrm{HO}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{OH}$$

Ethylene glycol *Oxalic acid*

This compound crystallizes as its calcium salt, calcium oxalate (CaC_2O_4), in the kidneys, leading to renal damage. Such injury can lead to kidney failure and death. As with methanol poisoning, the usual treatment for ethylene glycol poisoning is ethanol, administered to load up and thus block the liver enzymes from catalyzing the conversion of ethylene glycol to oxalic acid.

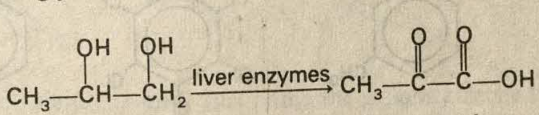
Another common dihydric alcohol is propylene glycol.



$$\mathrm{CH_3}\underset{\mathrm{OH}}{\mathrm{CH}}-\underset{\mathrm{OH}}{\mathrm{CH_2}}$$

The physical properties of this compound are quite similar to those of ethylene glycol (**table 16.4**). Its physiological properties, however, are quite different.

Propylene glycol is essentially nontoxic, and it can be used as a solvent for drugs. It is also used as a moisturizing agent for foods. Like other alcohols, propylene glycol can be oxidized by liver enzymes.

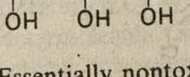


$$\mathrm{CH_3}-\overset{\mathrm{OH}}{\mathrm{CH}}-\overset{\mathrm{OH}}{\mathrm{CH_2}} \xrightarrow{\text{liver enzymes}} \mathrm{CH_3}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{OH}$$

Propylene glycol *Pyruvic acid*

In this case, however, the product is pyruvic acid, a normal intermediate in carbohydrate metabolism.

Glycerol (glycerin) is the most important trihydric alcohol.



$$\underset{\mathrm{OH}}{\mathrm{CH_2}}-\underset{\mathrm{OH}}{\mathrm{CH}}-\underset{\mathrm{OH}}{\mathrm{CH_2}}$$

It is a sweet, syrupy liquid. Essentially nontoxic, it is a product of the hydrolysis of fats (chapter 29).

Table 16.4
Properties of some polyhydric alcohols

Name	*Formula*	*Boiling Point (in degrees Celsius)*	*Solubility in Water*
Ethylene glycol	CH_2OHCH_2OH	198	∞
Propylene glycol	$CH_3CHOHCH_2OH$	188	∞
Glycerol	$CH_2OHCHOHCH_2OH$	290 (decomposes)	∞
Sorbitol	$CH_2OH(CHOH)_4CH_2OH$	(Solid)	∞

Certainly the carbohydrates are the most important polyhydric alcohols of all. We shall consider the structure of these compounds in chapter 22 and their metabolism in chapter 30.

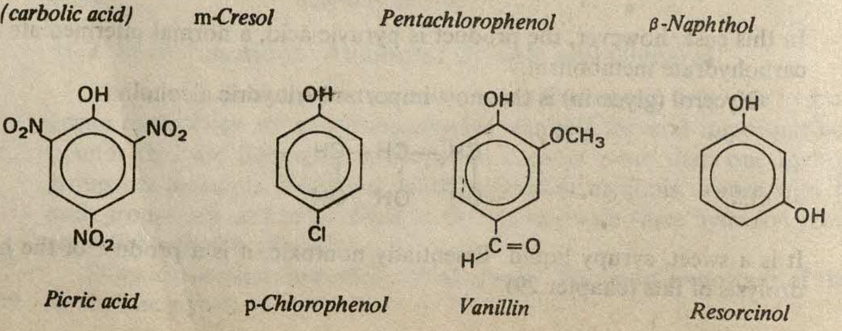
16.8 The Phenols: Weapons in the War on Germs

Compounds with a hydroxyl group attached directly to an aromatic ring are called *phenols*. The parent compound, C_6H_5OH, is itself called phenol. Other compounds may be named as derivatives of phenol, but most of those of interest to us are best known by special, nonsystematic names. A variety of phenols of interest are shown in **figure 16.6.**

The phenols generally are solids with low melting points or oily liquids at room temperature. Most are only sparingly soluble in water. By their very nature, phenols never contain fewer than six carbons. They have found wide use as germicides or antiseptics (substances which kill microorganisms on living tissue) and as disinfectants (substances intended to kill microorganisms on furniture, fixtures, floors, and around the house in general).

The first widely used antiseptic was phenol itself, which was also called

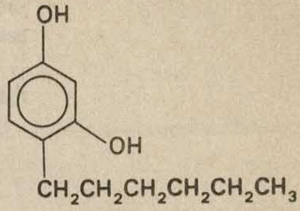
Figure 16.6 Some phenols of interest. *p*-Chlorophenol is a topical antiseptic, pentachlorophenol is an algicide and a herbicide, *β*-naphthol is a dye intermediate, picric acid is an explosive, and resorcinol is a chemical intermediate.



Phenol (carbolic acid) m-*Cresol* *Pentachlorophenol* *β-Naphthol*

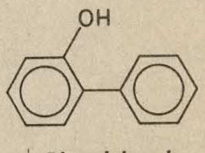
Picric acid p-*Chlorophenol* *Vanillin* *Resorcinol* carbolic acid. Joseph Lister used it for antiseptic surgery in 1867. Unfortunately, phenol doesn't kill only undesirable microorganisms. It kills all types of cells. Applied to the skin, it can cause severe burns. In the bloodstream it is a systemic poison, that is, one which is carried to and affects all parts of the body. Its severe side effects led to searches for safer antiseptics, a number of which have been found.

One of the most active phenolic antiseptics is 4-*n*-hexylresorcinol. It is much more powerful than phenol as a germicide and has fewer undesirable side effects. Indeed, it is safe enough to be used as the active ingredient in some mouthwashes.



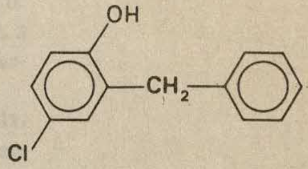
4-n-*Hexylresorcenol*

Prominent among disinfectants are the compounds *o*-phenylphenol and *o*-benzyl-*p*-chlorophenol. These compounds are the main active ingredients in preparations such as *Lysol.*

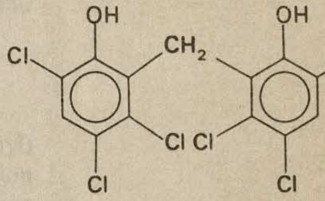


o-*Phenylphenol*

Hexachlorophene was once widely used in germicidal cleaning solutions (*Phisohex*) and as an ingredient in deodorant soaps and other cosmetics. Structurally, hexachlorophene is a phenol, but it also resembles DDT and the PCBs (chapter 15). In the United States, products contained at most 3% hexachlorophene. The compound was generally considered a safe and effective antibacterial agent. In September 1972, however, the picture changed rapidly. An outbreak of neurological disease among infants in northeastern France was traced to a baby powder called *Bébé* which contained over 20% hexachlorophene. Over 30 of the infants died. The U.S. Food and Drug Administration acted quickly. Hexachlorophene was banned from all products intended for over-the-counter sales. It is still available for prescription use and for use in hospitals—in concentrations not to exceed 3%.



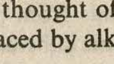
o-*Benzyl*-p-*chlorophenol*

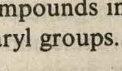


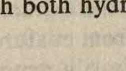
Hexachlorophene

16.9 The Ethers: Structures and Names

Alcohols and phenols may be considered derivatives of water in which one of the hydrogen atoms has been replaced by an alkyl or an aryl group. *Ethers* may be thought of as compounds in which both hydrogens of water have been replaced by alkyl or aryl groups.







Simple ethers are simply named. Just name the groups attached to oxygen and then add the generic name *ether* (**figure 16.7**). For symmetrical ethers (those in which both organic groups are identical), the group name should be preceded by the prefix *di-*, although the prefix is frequently dropped in common usage. The names *methyl ether* and *dimethyl ether* refer to the same compound, but the latter is preferred.

16.10 Properties of Ethers

Ether molecules have no hydrogen atom on oxygen; hence, molecules in the pure liquid are incapable of intermolecular hydrogen bonding. Given their molecular weight, then, the ethers have quite low boiling points. Indeed, ethers have boiling points about the same as those of alkanes of comparable molecular weight. For example, diethyl ether (whose molecular

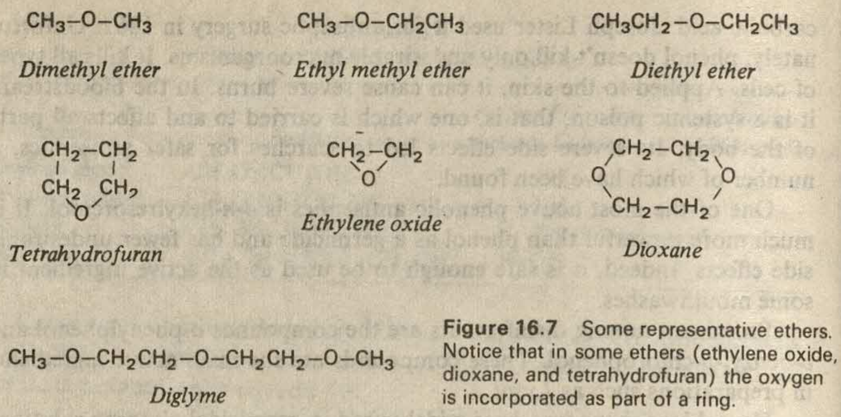
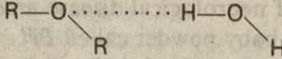


Figure 16.7 Some representative ethers. Notice that in some ethers (ethylene oxide, dioxane, and tetrahydrofuran) the oxygen is incorporated as part of a ring.

weight is 74) boils at 35 °C, and pentane (whose molecular weight is 72) boils at 36 °C. Ether molecules do have an oxygen atom, however. They can participate in hydrogen bonds if some other kind of molecule, such as water, will supply the appropriate kind of hydrogen.



Consequently, the ethers have about the same water solubilities as their isomeric alcohols. Both *n*-butyl alcohol and diethyl ether have the molecular formula $C_4H_{10}O$ (i.e., the ether and alcohol are isomers), and both are soluble to the extent of about 8 g in 100 g of water.

Chemically, the ethers are quite inert. Like the alkanes, they do not react with the usual oxidizing agents, reducing agents, or bases. The inertness of ethers makes them excellent solvents for organic materials. Diethyl ether is often used in the extraction of organic compounds from plant and animal materials or from mixtures of organic and inorganic substances. The volatile ether is then easily removed by evaporation, and the desired organic components are left behind. Dioxane and tetrahydrofuran (see **figure 16.7**) are also important organic solvents.

Diethyl ether is perhaps best known to the public as a general anesthetic.* When vapors of this volatile liquid are inhaled, the compound acts as a central nervous system (CNS) depressant. As side effects it may produce nausea, vomiting, and respiratory arrest. Just as the word *alcohol* is sometimes used to designate ethyl alcohol, the word *ether* is often used to refer to diethyl ether.

Use of diethyl ether in the laboratory or hospital produces unusual hazards. The compound is quite volatile and extremely flammable. The vapors form an explosive mixture with air. They are also heavier than air and can travel long distances along a tabletop or the floor to reach a flame or spark and set off an explosion. Ether fires cannot be extinguished with water because the ether is less dense than water and will float on top of it. The use of carbon dioxide fire extinguishers is recommended.

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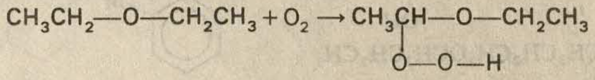
*A general anesthetic produces unconsciousness and renders one insensitive to pain.

Still another hazard with ethers is that, upon standing, they react with oxygen from the air to form peroxides.



$$CH_3CH_2\text{—}O\text{—}CH_2CH_3 + O_2 \rightarrow CH_3\underset{\underset{\displaystyle O\text{—}O\text{—}H}{|}}{C}H\text{—}O\text{—}CH_2CH_3$$

Diethyl ether *A peroxide*

These peroxides are less volatile than the ether and are concentrated in the residue left behind during a distillation or evaporation. But these concentrated peroxides are highly explosive and sensitive to both shock and heat. Hospitals avoid these problems by buying only those amounts of ether sufficient for immediate use and by keeping containers tightly closed and away from strong light, which catalyzes peroxide formation. Ethers suspected of containing peroxides should be treated with a reducing agent (as well as a great deal of respect). The peroxides are destroyed by reagents such as alkaline ferrous sulfate solution.

While members of a family of organic compounds generally have similar properties, there are usually some surprises, too. The ethers are no exception. Research workers came rather early to suspect that some polycyclic aromatic hydrocarbons (chapter 14) and aromatic amines (chapter 19) would exhibit carcinogenic properties; they were quite surprised to find that the chlorine-containing ether

$$Cl\text{—}CH_2\text{—}O\text{—}CH_2\text{—}Cl$$

was also a potent carcinogen. This compound, called bis(chloromethyl) ether* (BCME), causes malignancy in laboratory animals upon application to the skin or subcutaneous injection. Lung cancer is induced in mice by as little as 0.1 ppm of BCME in air. Epidemiological studies strongly suggest that occupational exposure to BCME causes lung cancer in humans.

Chloromethyl methyl ether (CH_3OCH_2Cl) is also thought to be a human carcinogen, although workers in whom malignancies have been found may also have been exposed to bis(chloromethyl) ether at the same time. These two ethers are among the dozen or more carcinogens rigidly regulated by the Occupational Safety and Health Administration (OSHA).

Problems

1. What is a functional group? What is the functional group in alcohols? In alkenes?

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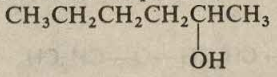
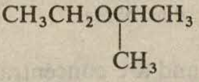
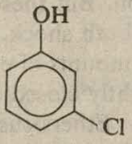
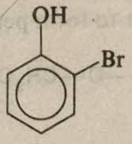
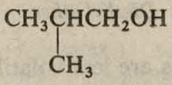
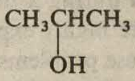
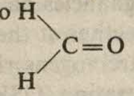
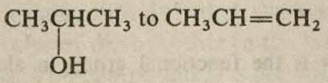
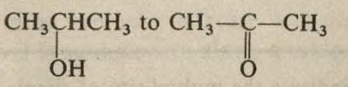
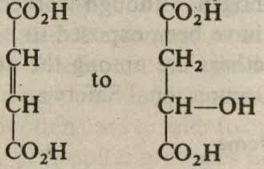
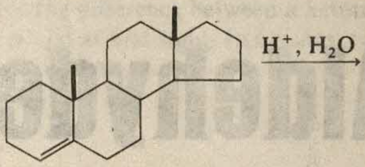
*The prefixes *di-*, *tri-*, and so on indicate the multiplicity of simple groups such as chloro or methyl groups. The prefixes *bis-*, *tris-*, and so on are used to indicate the multiplicity of complex groups such as chloromethyl (—CH_2Cl).

2. Write structural formulas for the eight isomeric pentyl alcohols. (Hint: Three are derived from *n*-pentane, four are derived from isopentane, and one is derived from neopentane.)
3. Classify the alcohols in problem 2 as primary, secondary, or tertiary.
4. Name these compounds.
   a. 
   $CH_3CH_2CH_2CH_2\underset{\underset{\displaystyle OH}{|}}{C}HCH_3$
   b. $CH_3CH_2CH_2OCH_2CH_2CH_3$
   c. 
   $CH_3CH_2O\underset{\underset{\displaystyle CH_3}{|}}{C}HCH_3$
   d. 
   e. 
   f. 
   $CH_3\underset{\underset{\displaystyle CH_3}{|}}{C}HCH_2OH$
   g. 
   $CH_3\underset{\underset{\displaystyle OH}{|}}{C}HCH_3$
   h. $CH_3CH_2CH_2CH_2CH_2CH_2OH$
5. Write structural formulas for the following.
   a. *tert*-butyl methyl ether
   b. *p*-iodophenol
   c. propylene glycol
   d. glycerol
   e. 4-methyl-2-hexanol
   f. *sec*-butyl alcohol
   g. *n*-pentyl alcohol
   h. 3-heptanol
   i. diisopropyl ether
   j. 2,2-dimethyl-1-propanol
   k. carbolic acid
6. Give the IUPAC names for the compounds referred to by these names.
   a. grain alcohol b. wood alcohol c. rubbing alcohol
   Which is most toxic? Which is least toxic?
7. What is denatured alcohol? Why is some alcohol denatured?
8. Is 90-proof liquor the product of simple fermentation, or should it be called distilled spirits?
9. Why is methanol so much more toxic to humans than ethanol?
10. Methanol is not particularly toxic to rats. If methanol were newly discovered and tested for toxicity in laboratory animals, what would you conclude about its safety for human consumption?
11. Why is ethylene glycol so much more toxic to humans than propylene glycol?
12. What chemical compound is used in the treatment of acute methanol or ethylene glycol poisoning? How does it work?
13. Classify each of these conversions as oxidation, dehydration, or hydration.
   a. CH_3OH to 
   b. 
   $CH_3\underset{\underset{\displaystyle OH}{|}}{C}HCH_3$ to $CH_3CH{=}CH_2$
   c. 
   $CH_3\underset{\underset{\displaystyle OH}{|}}{C}HCH_3$ to $CH_3{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}CH_3$
   d. 
   $\begin{array}{c} CO_2H \\ | \\ CH \\ \| \\ CH \\ | \\ CO_2H \end{array}$ to $\begin{array}{c} CO_2H \\ | \\ CH_2 \\ | \\ CH{-}OH \\ | \\ CO_2H \end{array}$
   e. CH_3OH to $CH_3{-}O{-}CH_3$
14. Each of the butyl alcohols is treated with potassium dichromate in acid. Draw the product (if any) expected from each of the four isomeric alcohols.
15. Write an equation for the dehydration of 1-propanol to yield an alkene.
16. Write an equation for the dehydration of 1-propanol to yield an ether.
17. What is Markovnikov's rule?

18. What is the product of each of the following reactions?

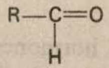
a. $CH_2{=}CHCH_2CH_3 \xrightarrow{H^+,\ H_2O}$

b.



19. Without consulting the tables, arrange the members of each group in order of increasing boiling point.
    a. ethanol, 1-propanol, methanol
    b. *n*-butane, ethylene glycol, 1-propanol
    c. diethyl ether, propylene glycol, 1-butanol
20. Primary alcohols can be oxidized to aldehydes. The aldehydes will boil out of the oxidation reaction mixture at a temperature which will leave the unreacted alcohol behind. Explain how this difference in boiling points could be predicted from the structure of the following compounds.

$R{-}CH_2OH$



$$R{-}\underset{\displaystyle H}{\underset{|}{C}}{=}O$$

21. Without consulting the tables, arrange the members of each group in order of increasing solubility in water.
    a. methanol, 1-butanol, 1-octanol
    b. *n*-pentane, propylene glycol, diethyl ether

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9. "More Molecules Found in Interstellar Space," *Chemical and Engineering News*, 4 November 1974, p. 4. There is ethanol and dimethyl ether out there; indeed, there are 1 × 10^{28} fifths of 80-proof booze in Sagitarrius B2 alone.
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chapter 17

Aldehydes and Ketones

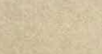
What do certain hormones, vanilla flavor, a biological tissue preservative, and fresh cucumbers have in common? A carbonyl functional group, that's what. The carbonyl group is characteristic of aldehydes and ketones, the families we shall consider in this chapter. As the opening list indicates, this functional group and these two families of compounds are found in a most diverse company of products. Both the tempting aromas associated with cinnamon, vanilla, and fresh, buttered baked goods and the sickeningly sweet smell of some rancid foods are associated with the carbonyl group. The chemistry of the group is as interesting as its physical properties, and we shall spend considerable time studying some aspects of that chemistry.

Figure 17.1 The carbonyl functional group is found in many diverse materials.

The aldehydes and ketones offer us an opportunity to study the carbonyl group in its simplest surroundings. In the next chapter we shall consider somewhat more complicated functional groups incorporating the carbonyl group. And we shall ultimately find ourselves running into this ubiquitous grouping of atoms in carbohydrates, fats, proteins, nucleic acids, hormones, vitamins, and the host of organic compounds critical to the functioning of living systems. But first things first. Let's begin by focusing on the carbonyl group in aldehydes and ketones.

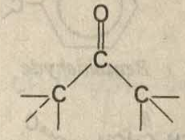
17.1 The Carbonyl Group: A Carbon-Oxygen Double Bond

We first encountered a functional group containing a double bond in the alkenes. In the members of this family, two carbon atoms share four electrons (two pairs) to form a carbon-carbon double bond. In the alcohols, we saw a functional group in which an oxygen atom was attached to a carbon atom. The carbonyl group incorporates a feature of each of these other functional groups. It involves carbon bonded to oxygen and a double bond—a carbon-oxygen double bond.

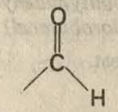


The carbonyl double bond, like the alkene double bond, tends to undergo addition reactions. But, unlike the alkene double bond, it involves an oxygen atom and is highly polar. That polarity confers certain special properties on aldehydes and ketones.

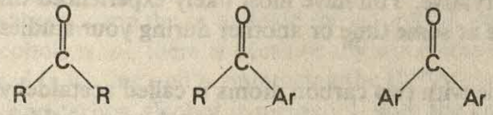
What is the difference between a ketone and an aldehyde? It appears to be rather trivial at first sight. In *ketones*, two carbon groups are attached to the carbonyl carbon.



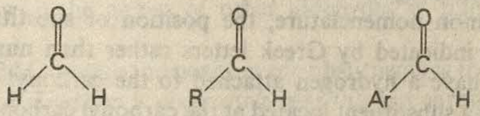
In *aldehydes*, at least one of the attached groups must be hydrogen.



Thus, these general formulas all represent ketones.



These compounds are all aldehydes.

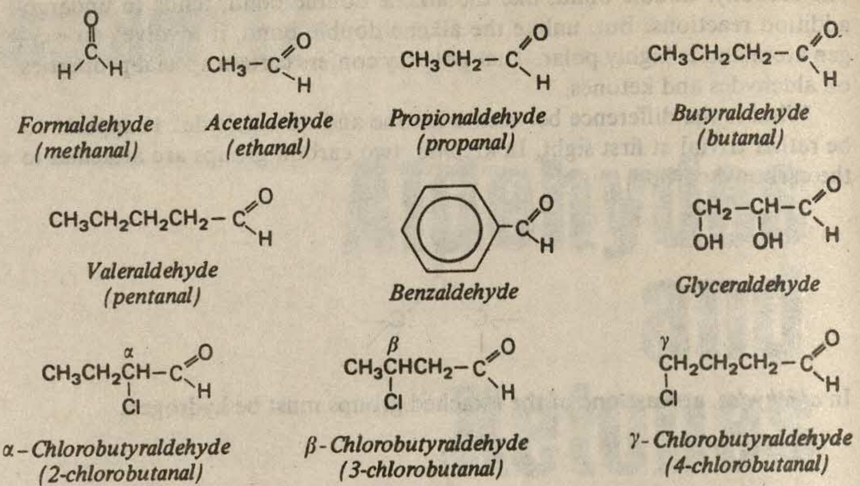


Aldehydes and ketones share many common properties, as one might expect for compounds with the same functional group. But they are different in other respects, different enough to warrant their classification into two families.

17.2 How to Name the Common Aldehydes

As with most compounds isolated from natural sources, aldehydes came to be known by common names long before IUPAC rules were set up. And the common aldehyde names were adapted from common names for the carboxylic acids. This common naming system is, in many respects, as organized as the official IUPAC system. For the present, we shall simply give the common names of aldehydes of interest and cite one of the "rules" of the common system. In the next chapter, the derivation of the common names will be discussed.

The simplest aldehyde, and the only one with two hydrogens attached to the carbonyl group, contains only one carbon atom and is known as



Formaldehyde (methanal)

Acetaldehyde (ethanal)

Propionaldehyde (propanal)

Butyraldehyde (butanal)

Valeraldehyde (pentanal)

Benzaldehyde

Glyceraldehyde

α-Chlorobutyraldehyde (2-chlorobutanal)

β-Chlorobutyraldehyde (3-chlorobutanal)

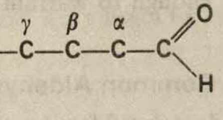
γ-Chlorobutyraldehyde (4-chlorobutanal)

Figure 17.2 Some aldehydes of interest.

formaldehyde. This compound is a gas at room temperature, but it is available as a 40% aqueous solution called formalin. This solution is a familiar biological preservative. You have most likely experienced the pungent odor of formaldehyde at some time or another during your studies in the biology laboratory.

The aldehyde with two carbon atoms is called **acetaldehyde**. Those with three, four, and five carbon atoms are named **propionaldehyde**, **butyraldehyde**, and **valeraldehyde**, respectively. These aldehydes and a few others of interest are shown in **figure 17.2.**

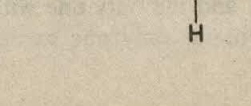
In the common nomenclature, the position of substituents along the parent chain is indicated by Greek letters rather than numbers. Since an aldehyde must have a hydrogen attached to the carbonyl group, it is not possible to have a substituent located at the carbonyl carbon (all of its bonds are already in use). Therefore, the first Greek letter is assigned to the carbon atom *next to* the carbon in the carbonyl group.



There is rarely a need to specify a position beyond these. This system is illustrated by the three chlorobutyraldehydes in **figure 17.2.**

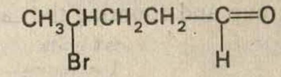
Example 17.1 Write the structural formula for γ-bromovaleraldehyde.

Valeraldehyde has five carbon atoms.



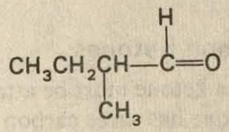
$$\overset{}{C}-\overset{\gamma}{C}-\overset{\beta}{C}-\overset{\alpha}{C}-\underset{H}{\underset{|}{C}}{=}O$$

The gamma carbon is the third from the functional group (not counting the carbonyl carbon). Thus, the structure is



$$\mathrm{CH_3\underset{\displaystyle |\atop Br}{C}HCH_2CH_2{-}\underset{\displaystyle |\atop H}{C}{=}O}$$

Example 17.2 Name the compound

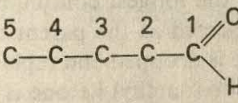


$$\mathrm{CH_3CH_2\underset{\displaystyle |\atop CH_3}{C}H{-}\overset{\displaystyle H\atop |}{C}{=}O}$$

The compound may be named as a derivative of butyraldehyde (longest continuous chain including the carbonyl carbon contains four carbon atoms). There is a methyl group on the alpha carbon, the first one after the carbonyl carbon. A suitable name is α-methylbutyraldehyde.

The IUPAC names of aldehydes are derived from those of the corresponding alkanes. Select the longest continuous chain of carbon atoms that contains the functional group. Take the name of the alkane with that number of carbon atoms, drop the *-e*, and add the ending *-al*. Because the IUPAC ending for alcohols is *-ol*, there is occasionally some confusion unless great care is exercised in writing and pronouncing the IUPAC names of these two families. The one-carbon alcohol is methanol, with the ending pronounced like the *ol* in old. The one-carbon aldehyde is methanal, with the ending pronounced like the man's name *Al*. IUPAC names of the first five aldehydes, along with the names of other aldehydes of interest, are given in **figure 17.2.**

In the IUPAC system the position of substituents is indicated by a number. The carbonyl carbon is *always* taken as the first carbon.

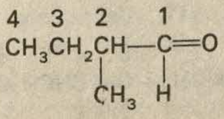


$$\overset{5}{\mathrm{C}}-\overset{4}{\mathrm{C}}-\overset{3}{\mathrm{C}}-\overset{2}{\mathrm{C}}-\overset{1}{\mathrm{C}}\begin{smallmatrix}{/\!\!/}\mathrm{O}\\ \diagdown\mathrm{H}\end{smallmatrix}$$

Note that the second carbon in the IUPAC system corresponds to the alpha carbon in the common system.

Example 17.3 What is the IUPAC name for the compound in example 17.2?

There are four carbon atoms in the longest continuous chain. There is a methyl group on the second (alpha) carbon.

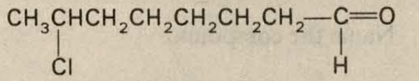


$$\mathrm{\overset{4}{C}H_3\overset{3}{C}H_2\underset{\displaystyle |\atop CH_3}{\overset{2}{C}}H{-}\underset{\displaystyle |\atop H}{\overset{1}{C}}{=}O}$$

The name is 2-methylbutanal.

Example 17.4 Write the structure for 7-chlorooctanal.

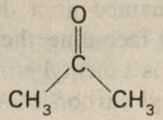
There are eight carbon atoms in the longest continuous chain. There is a chlorine atom on the seventh carbon atom, numbering from the functional group and counting the carbonyl carbon as the first carbon atom.



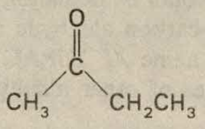
$$\mathrm{CH_3\underset{\underset{Cl}{|}}{C}HCH_2CH_2CH_2CH_2CH_2{-}\underset{\underset{H}{|}}{C}{=}O}$$

17.3 Naming the Common Ketones

The carbonyl group in a ketone must be attached to two carbon groups. Therefore, the simplest ketone has three carbon atoms.



It is known far and wide by the name *acetone*. The name is unique and does not correspond to the first in a series of similar common names. Generally, ketones are given common names consisting of the names of the groups attached to the carbonyl group, followed by the word ketone. (Note the similarity to the naming of ethers.) Another name for acetone, then, is dimethyl ketone. With four carbon atoms, we have ethyl methyl ketone.

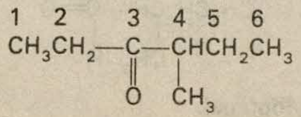


If names for the groups attached to the carbonyl group are known, this common naming system can be applied.

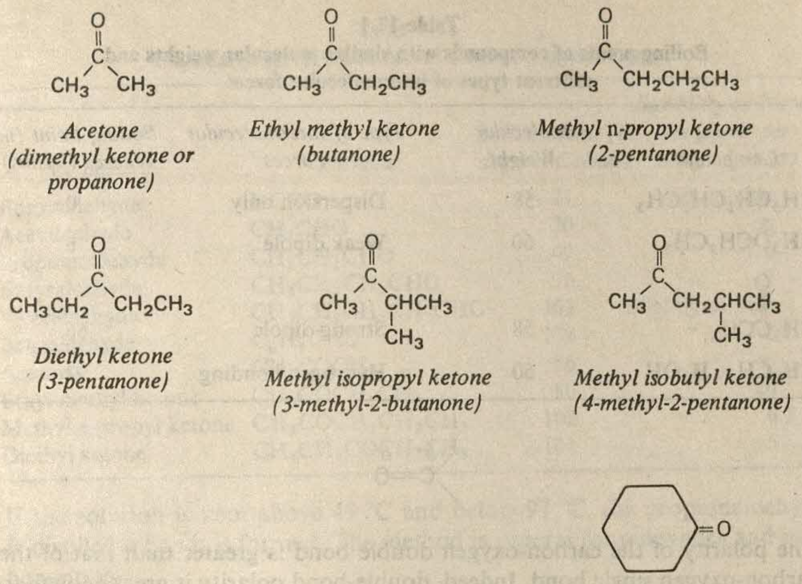
In the IUPAC system, the longest continuous chain to which the oxygen is doubly bonded is selected as the parent chain. The *-e* ending of the corresponding alkane name is dropped and replaced with *-one*. Acetone thus becomes propanone, and ethyl methyl ketone is called butanone. In higher ketones, a number indicates the position of the doubly bonded oxygen. The locations of any substituents are also indicated by numbers. **Figure 17.3** shows an assortment of ketones of interest and lists both IUPAC and common names.

Example 17.5 Write the structure for 4-methyl-3-hexanone.

The longest chain has six carbon atoms with a doubly bonded oxygen located at the third carbon and a methyl group at the fourth carbon.



$$\mathrm{\overset{1}{CH_3}\overset{2}{CH_2}{-}\underset{\underset{O}{\|}}{\overset{3}{C}}{-}\underset{\underset{CH_3}{|}}{\overset{4}{C}}H\overset{5}{C}H_2\overset{6}{C}H_3}$$



Acetone (dimethyl ketone or propanone)

Ethyl methyl ketone (butanone)

Methyl n-*propyl ketone (2-pentanone)*

Diethyl ketone (3-pentanone)

Methyl isopropyl ketone (3-methyl-2-butanone)

Methyl isobutyl ketone (4-methyl-2-pentanone)

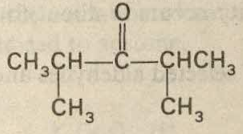
Cyclohexanone

Figure 17.3 Some common ketones.

Example 17.6 Give a common name for the ketone in example 17.5.

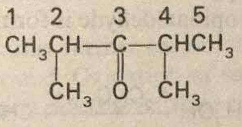
The two alkyl groups attached to the carbonyl group are ethyl and *sec*-butyl. The common name is *sec*-butyl ethyl ketone.

Example 17.7 Write the structure for diisopropyl ketone.



$$\mathrm{CH_3\underset{\displaystyle CH_3}{\underset{|}{CH}}-\overset{\displaystyle O}{\overset{\|}{C}}-\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3}$$

Example 17.8 What is the IUPAC name for the ketone in example 17.7?



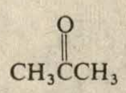
$$\mathrm{\overset{1}{CH_3}\underset{\displaystyle CH_3}{\underset{|}{\overset{2}{CH}}}-\underset{\displaystyle O}{\underset{\|}{\overset{3}{C}}}-\underset{\displaystyle CH_3}{\underset{|}{\overset{4}{CH}}}\overset{5}{CH_3}}$$

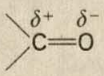
The name is 2,4-dimethyl-3-pentanone.

17.4 Physical Properties of Aldehydes and Ketones

The carbon and oxygen of the carbonyl group share two pairs of electrons, but they do not share them equally. The electronegative oxygen has a much greater attraction for the bonding pairs. Thus, the electron density is heavier at the oxygen end of the bond and lighter at the carbon end. The carbon is left with a partial positive charge; the oxygen, with a partial negative charge.

Table 17.1
Boiling points of compounds with similar molecular weights and different types of intermolecular forces

Compound	*Molecular Weight*	*Type of Intermolecular Forces*	*Boiling Point (in degrees Celsius)*
$CH_3CH_2CH_2CH_3$	58	Dispersion only	0
$CH_3OCH_2CH_3$	60	Weak dipole	6
 $CH_3\overset{\overset{O}{\Vert}}{C}CH_3$	58	Strong dipole	56
$CH_3CH_2CH_2OH$	60	Hydrogen bonding	97



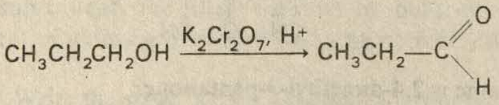
The polarity of the carbon-oxygen double bond is greater than that of the carbon-oxygen single bond. Indeed, double-bond polarity is great enough to affect the boiling points of aldehydes and ketones, whereas the polar single bonds in ethers (chapter 16) have little effect on boiling points (**table 17.1**). Such dipolar forces, however, are still not comparable to the hydrogen bonding that exists between molecules of an alcohol.

Although there can be no intermolecular hydrogen bonding in pure aldehydes or ketones,* there can be hydrogen bonds to water molecules. These families are thus about as soluble in water as alcohols of comparable weight. The borderline of solubility occurs at about four carbon atoms per oxygen atom.

Physical properties of selected aldehydes and ketones are summarized in **table 17.2.**

17.5 How to Make Aldehydes and Ketones

Careful oxidation of a primary alcohol gives an aldehyde (chapter 16). For example, when *n*-propyl alcohol is warmed with an acidic solution of potassium dichromate, propionaldehyde is formed.



n-*Propyl alcohol*
(boiling point, 97 °C)

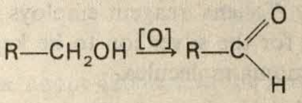
Propionaldehyde
(boiling point, 49 °C)

*Remember that the hydrogen which must be attached to the carbonyl group in an aldehyde is attached to the carbon atom, not the oxygen, of the functional group. Such a hydrogen is not capable of intermolecular hydrogen bonding.

Table 17.2
Physical properties of selected aldehydes and ketones

Compound	*Formula*	*Boiling Point (in degrees Celsius)*	*Solubility in Water (in grams per 100 g of water)*
Formaldehyde	$HCHO$	−21	Very soluble
Acetaldehyde	CH_3CHO	20	∞
Propionaldehyde	CH_3CH_2CHO	49	16
Butyraldehyde	$CH_3CH_2CH_2CHO$	76	7
Valeraldehyde	$CH_3CH_2CH_2CH_2CHO$	103	Slightly soluble
Benzaldehyde	C_6H_5CHO	178	0.3
Acetone	CH_3COCH_3	56	∞
Ethyl methyl ketone	$CH_3COCH_2CH_3$	80	26
Methyl *n*-propyl ketone	$CH_3COCH_2CH_2CH_3$	102	6.3
Diethyl ketone	$CH_3CH_2COCH_2CH_3$	101	5

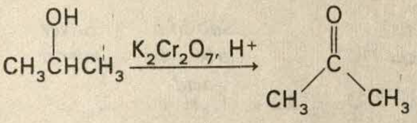
If the solution is kept above 49 °C and below 97 °C, the propionaldehyde is distilled off as it is formed. The method is general for aldehydes and may be written



A primary alcohol   *An aldehyde*

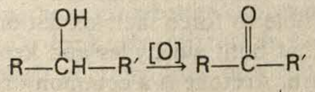
where, once again, the symbol [O] represents oxidation.

Ketones are formed by the oxidation of secondary alcohols. For example, isopropyl alcohol is oxidized to acetone.



Isopropyl alcohol   *Acetone*

Unlike aldehydes, ketones resist further oxidation. It is not necessary to remove the ketone as it is formed. Oxidation of secondary alcohols is a general method for the preparation of ketones. The process may be represented as



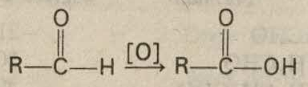
$$R{-}\overset{\overset{\displaystyle OH}{|}}{C}H{-}R' \xrightarrow{[O]} R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}R'$$

A secondary alcohol   *A ketone*

Chemists have many other ways of introducing carbonyl groups into molecules. Our discussion, though, is limited to oxidation processes because these are similar to the reactions occurring in our bodies.

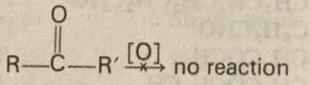
17.6 Oxidation of Aldehydes: Professor Tollens' Silver Mirror

Aldehydes are themselves readily oxidized, yielding carboxylic acids. Ketones are resistant to oxidation.



$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}H \xrightarrow{[O]} R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OH$$

An aldehyde *Carboxylic acid*



$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}R' \overset{[O]}{\not\longrightarrow} \text{no reaction}$$

A ketone

The aldehydes are, in fact, among the most easily oxidized of organic compounds, and this fact helps chemists identify them. Through the use of oxidizing agents, aldehydes can be distinguished not only from ketones but also from alcohols if the reagent is gentle enough. One such test reagent was invented by Professor Bernhard Tollens (1841–1918) at the University of Göttingen in Germany. Tollens' reagent employs silver ion as the mild oxidizing agent. In order for the silver ion to be kept in solution, it must be complexed by two ammonia molecules.

$$H_3N{-}Ag^+{-}NH_3$$

When Tollens' reagent oxidizes an aldehyde, the silver ion is reduced to free silver.

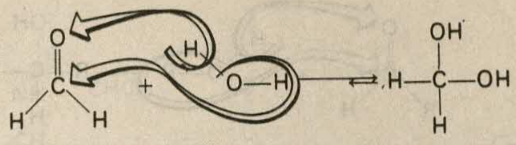
$$\underset{\substack{\textit{An}\\\textit{aldehyde}}}{RCHO} + \underset{\substack{\textit{Tollens'}\\\textit{reagent}}}{2\,Ag(NH_3)_2^+} + 2\,OH^- \longrightarrow \underset{\substack{\textit{Salt of a}\\\textit{carboxylic}\\\textit{acid}}}{RCOO^-} + \underset{\substack{\textit{Silver}\\\textit{mirror}}}{2\,Ag(s)} + NH_4^+ + 3\,NH_3 + H_2O$$

This silver, when deposited on a clean glass surface, produces a beautiful mirror. Indeed, mirrors are often silvered by means of the Tollens reaction. The reducing agent of choice is often the sugar glucose (which contains an aldehyde functional group) rather than a simple aldehyde. Ordinary ketones do not react with Tollens' reagent.

Although ketones are resistant to oxidation by ordinary laboratory oxidizing agents, it is possible to force their oxidation. And, in particular, it should be recognized that both aldehydes and ketones will undergo combustion, that is, will burn. Acetone is a common organic solvent. Neither it nor any other volatile, flammable organic solvent should be used around open flames, heating elements, or other sources of possible ignition.

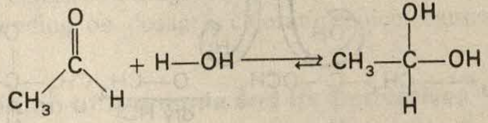
17.7 Hydrated Carbonyl Compounds: Formalin to Mickey Finn

Formaldehyde is a gas at room temperature, yet it dissolves readily in water. In fact, formaldehyde actually *reacts* with water.



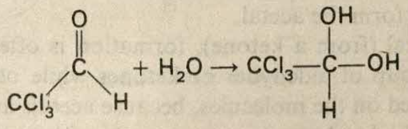
The process is an addition reaction, analogous to the hydration of the carbon-carbon double bond of an alkene. The net result is that a hydrogen from water is added to the carbonyl oxygen and a hydroxyl group from water becomes attached to the carbonyl carbon. The product is called a hydrate. It readily breaks down to re-form formaldehyde and water. At equilibrium at 20 °C, the hydrate predominates. Indeed, only 1 molecule in 10 000 exists as free formaldehyde. The other 9999 are in the form of the hydrate.

Acetaldehyde is also hydrated in aqueous solution, but to a lesser extent than formaldehyde.



Out of 10 000 molecules, about 4200 are in the form of the free aldehyde at equilibrium. Still, that leaves 5800 in the hydrated form. Generally, higher aldehydes and ketones are even less hydrated, existing primarily in the free aldehyde form at equilibrium in water.

In most cases, it is impossible to isolate the hydrates from solution. Attempts to do so result in loss of water and regeneration of the carbonyl group. An exception is the hydrate of trichloroacetaldehyde.

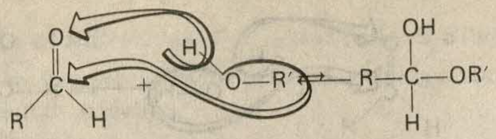


Trichloroacetaldehyde *Chloral hydrate*

The product, called chloral hydrate, is a stable crystalline solid. It is a powerful sedative and soporific (sleep-inducing drug). Chloral hydrate has had wide use in medicine. It is perhaps even better known in fictional mystery stories. Slipped into someone's drink, the mixture is called a "Mickey Finn" or "knockout drops." Such combinations of alcohol and chloral hydrate—two "downers"—are exceedingly dangerous. A little too much and the unfortunate victim may be put to sleep permanently.

17.8 The Addition of Alcohols: Hemiacetals and Acetals

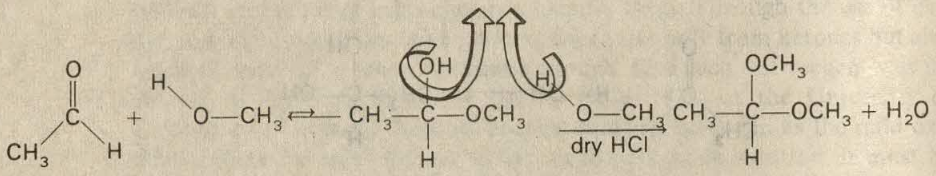
Alcohols add to the carbonyl group of aldehydes and ketones in much the same way as water.



The product, called a *hemiacetal,* is generally quite unstable. It readily reverts to the aldehyde and alcohol.

Hemiacetals are quite important in carbohydrate chemistry (chapter 22). Simple sugars, such as glucose, have aldehyde functional groups and alcohol groups on the same molecule. These interact to form intramolecular hemiacetals. Such cyclic hemiacetals are relatively stable. In aqueous solution they are frequently the predominant form of the sugar.

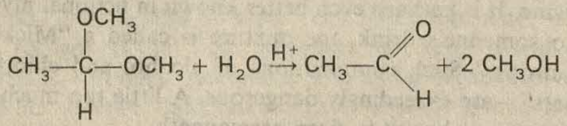
Hemiacetals can be made to react further with alcohols. If dry hydrogen chloride gas is bubbled into a solution of aldehyde in excess alcohol, an *acetal* is formed. The reaction for acetaldehyde and methanol is



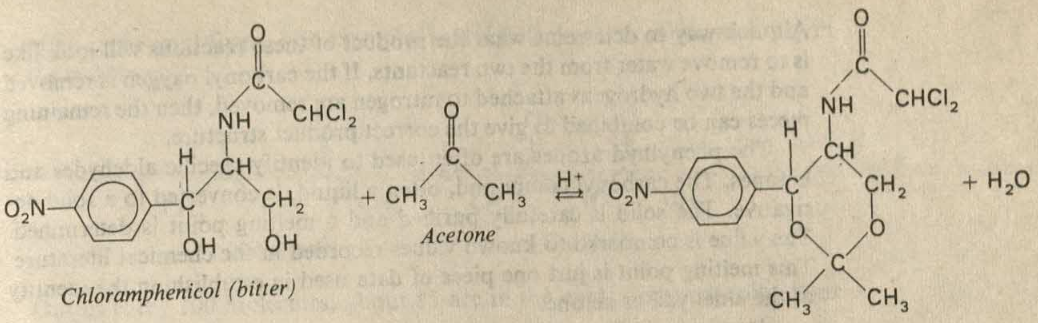
A hemiacetal *An acetal*

Unlike hemiacetals and hydrates, acetals are quite stable. They can be isolated in pure form. Notice that the second part of the reaction, the formation of the acetal from the hemiacetal, is analogous to the dehydration reaction which yields an ether (chapter 16). Thus, one first adds an alcohol molecule to the double bond of the aldehyde to form the hemiacetal. Then one removes the hydroxyl group of the hemiacetal and the hydrogen from the hydroxyl group of a second alcohol molecule and attaches the two remaining pieces together to form the acetal.

Acetal, or ketal (from a ketone), formation is often used to "protect" the functional group of aldehydes or ketones while other chemical operations are performed on the molecules, because acetals are resistant to oxidation whereas aldehydes themselves are not. An aldehyde could be converted to an acetal, an oxidation reaction could then be carried out on another part of the molecule, and finally the aldehyde could be regenerated from the acetal. The carbonyl group is easily regenerated by aqueous acid.



In an interesting application, the antibiotic chloramphenicol is treated with acetone and a protective cyclic ketal is formed which masks the bitter taste of the drug. Both of the alcohol hydroxyl groups required to form the ketal are attached to a single molecule in this use.



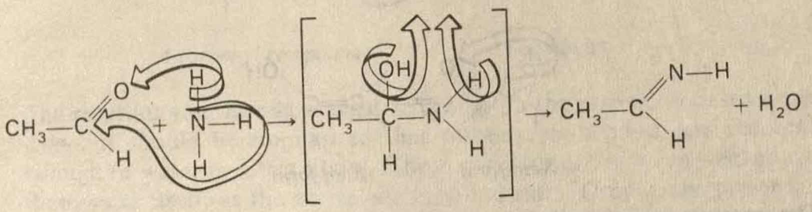
Chloramphenicol (bitter) *Acetone* *A cyclic ketal (not bitter)*

The cyclic ketal is converted back to the free chloramphenicol by acids in the digestive system.

Chloramphenicol is a powerful, but hazardous, antibiotic. It is used only when other, less dangerous, drugs are ineffective. In about 1 person in 20 000 to 40 000 (depending on dosage), chloramphenicol causes fatal aplastic anemia.

17.9 The Addition of Ammonia and Its Derivatives

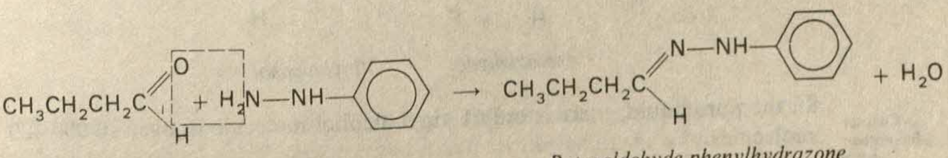
As with water and alcohols, ammonia readily adds to carbonyl compounds. The addition product is unstable. It eliminates a molecule of water to form a compound called an *imine*.



Unstable intermediate *An imine*

Such imines are highly reactive. They usually undergo further reaction, often to complex products.

Certain ammonia derivatives, however, react to give stable, often crystalline products. An example is phenylhydrazine. It reacts with aldehydes and ketones to give yellow to orange crystalline solids called phenylhydrazones. Butyraldehyde, for example, gives butyraldehyde phenylhydrazone.



Butyraldehyde *Phenylhydrazine* *Butyraldehyde phenylhydrazone*

A quick way to determine what the product of these reactions will look like is to remove water from the two reactants. If the carbonyl oxygen is removed and the two hydrogens attached to nitrogen are removed, then the remaining pieces can be combined to give the correct product structure.

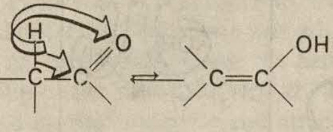
The phenylhydrazones are often used to identify specific aldehydes and ketones. The carbonyl compound, often a liquid, is converted to a solid derivative. The solid is carefully purified and a melting point is determined. The value is compared to known values recorded in the chemical literature. This melting point is just one piece of data used in establishing the identity of the aldehyde or ketone.

Reactions similar to the addition of ammonia are important in the biosynthesis of certain amino acids. In the presence of a nitrogen source and certain enzymes, a carbohydrate metabolite, for example, may be converted into an amino acid (chapter 32). In this way, the body can use carbohydrates as an ultimate source for some proteins.

A common dipstick test for ketones in urine (chapter 28) involves sodium nitroprusside, also known as sodium nitroferricyanide [$Na_2Fe(CN)_5NO$]. In alkaline media and in the presence of a nitrogen compound, this system gives a red to purple color if ketones are present.

17.10 Shifty Hydrogens: Tautomerism

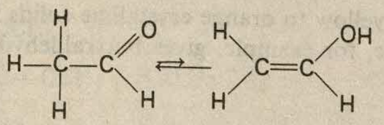
A carbonyl compound with a hydrogen atom on the alpha carbon exists in equilibrium with an isomeric form in which that hydrogen has shifted to the carbonyl oxygen atom.



Keto form *Enol form*

The isomeric form is called an *enol,* for it contains a double bond (alkene) and an alcohol functional group. This type of isomerism is what we call *tautomerism.*

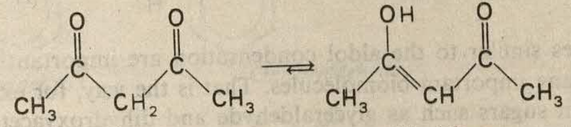
For simple aldehydes and ketones, the equilibrium lies very far toward the keto form. Consider as an example the equilibrium between acetaldehyde and its tautomer, vinyl alcohol.



Acetaldehyde *Vinyl alcohol*

In the pure liquid, there is only 1 vinyl alcohol molecule in over 10 000 000 molecules.

There are compounds in which a substantial portion of the molecules exist in the enol form. For example, acetylacetone exists predominantly in the enol form.



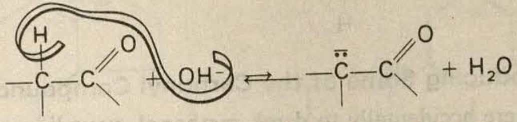
Keto form *Enol form*

Out of every 100 molecules, about 85 are in the enol form and only about 15 are in the keto form.

Keto-enol shifts are important in carbohydrate chemistry, also. Fructose, which has a ketone functional group, can rearrange to glucose, which has an aldehyde functional group, through tautomeric shifts (chapter 22).

17.11 Aldol Condensation: What Aldol Hath Joined Together . . .

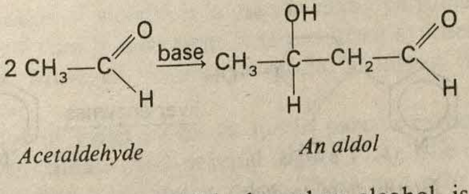
Generally, hydrogen attached to carbon has no appreciable acidity, that is, it tends to stay attached where it is. As the phenomenon of keto-enol tautomerism suggests, however, hydrogen atoms on an alpha carbon (i.e., on the carbon nearest the carbonyl group) are slightly acidic. They are sufficiently acidic to be pulled off by a strong base.



A carbonyl compound *A carbanion*

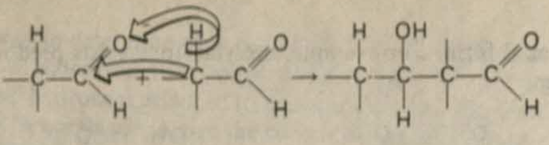
The resulting ion, having a negative charge on the carbon, is called a *carbanion*. It should be emphasized that carbonyl compounds are not acidic enough in water to affect litmus. These compounds are much weaker acids than water itself, as the above equation indicates. Only in the presence of a strong base can a significant number of molecules be converted to anions. Even then the equilibrium lies far in the direction of the un-ionized form.

The carbanions formed by the reaction of base with a carbonyl compound can add to other molecules of the aldehyde or ketone. This type of reaction, in which small molecules combine to form larger ones, is called a *condensation*. For acetaldehyde, the condensation may be written as

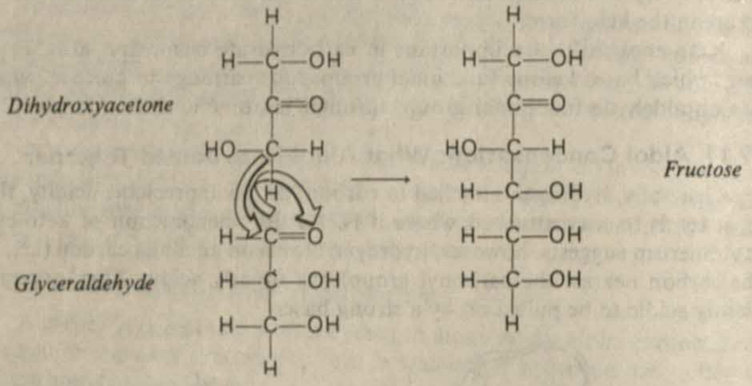


Acetaldehyde *An aldol*

The product, which is both an aldehyde and an alcohol, is called an *aldol*. The reaction is an *aldol condensation*. It can be viewed as the addition of one aldehyde molecule to the double bond of another.



Processes similar to the aldol condensation are important in the synthesis of many important biomolecules. That is the way, for example, that three-carbon sugars such as glyceraldehyde and dihydroxyacetone (in the form of phosphate esters) can be combined into six-carbon sugars such as fructose.

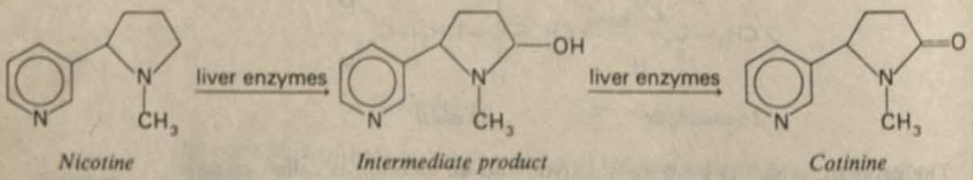


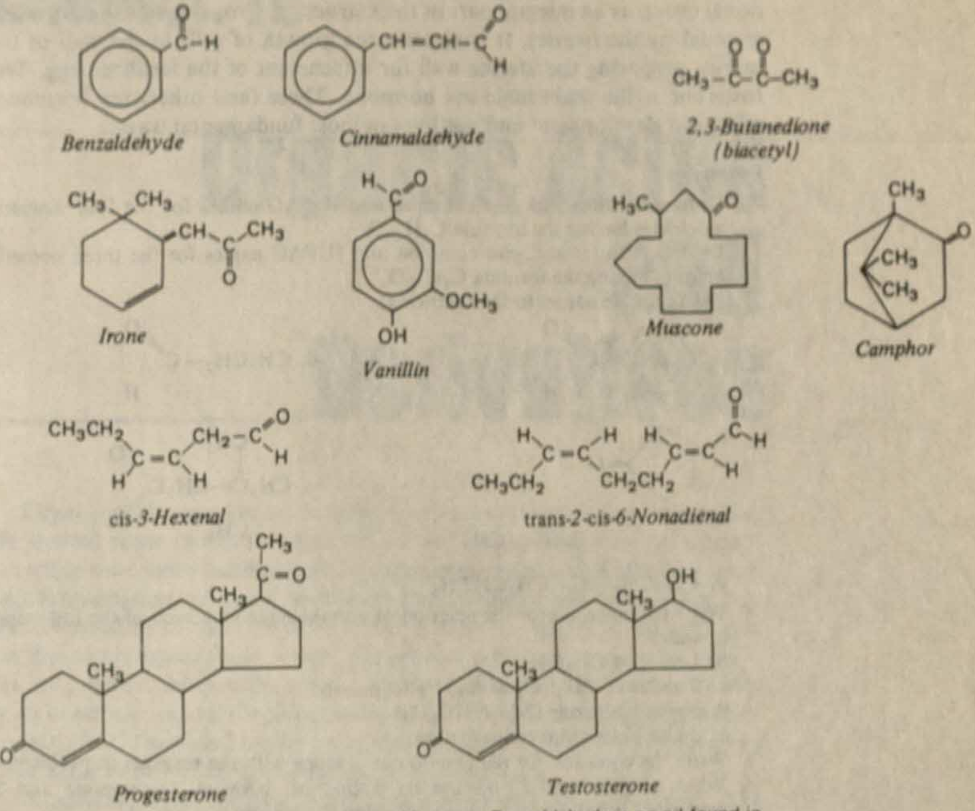
17.12 Introducing Some of the Carbonyl Compounds in Our Lives

If you were accidentally to drink methanol, your liver would oxidize it to formaldehyde (chapter 16). The formaldehyde would begin to "fix" your protein. It would, among other things, deactivate enzymes and render the lenses of your eyes opaque. In that way the methanol would cause blindness and—if you drank enough—death.

If you drank ethanol, your liver would oxidize it to acetaldehyde. This aldehyde is less toxic than formaldehyde. Further, acetaldehyde can be oxidized to acetic acid, which can be oxidized to carbon dioxide and water.

The liver oxidizes many compounds. Aldehydes and ketones are often intermediates—or even end products—of such oxidations. Nicotine, for example, is detoxified by oxidation. This occurs by way of an intermediate alcohol. The end product, cotinine, has little toxicity.





Benzaldehyde

Cinnamaldehyde

2,3-Butanedione (biacetyl)

Irone

Vanillin

Muscone

Camphor

cis-3-Hexenal

trans-2-cis-6-Nonadienal

Progesterone

Testosterone

Figure 17.4 Some interesting aldehydes and ketones. Benzaldehyde is an oil found in almonds. Cinnamaldehyde is oil of cinnamon. 2,3-Butanedione is responsible for the flavor of butter, and irone is responsible for the odor of violets. Vanillin, of course, gives vanilla its flavor. Muscone is musk oil, a common ingredient of perfumes. *cis*-3-Hexenal provides an herbal odor. *trans*-2-*cis*-6-Nonadienal gives a cucumber odor. Progesterone is a female sex hormone, and testosterone is a male sex hormone

Many familiar substances contain aldehydes or ketones as the active principles (**figure 17.4**). Benzaldehyde is the major component of oil of bitter almonds. Cinnamaldehyde is oil of cinnamon. Biacetyl contributes to the aroma and taste of fresh butter. Camphor is a bicyclic ketone. Irone is a ketone with the odor of violets; it is used in many perfumes. Vanillin is the active principle of vanilla flavoring; it is produced synthetically for use in imitation vanilla. Muscone, formed in special glands of the musk deer, is used in perfumes.

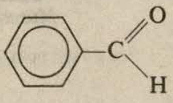
Even the odor of green leaves is due in part to carbonyl compounds. Most green leaves contain *cis*-3-hexenal (**figure 17.4**). The compound *trans*-2-*cis*-6-nonadienal has a cucumber odor. These and other carbonyl compounds (with related acetals, ketals, and alcohols) impart a "green," herbal odor to shampoos and other cosmetics.

Several of the steroid hormones (chapter 27) have the carbonyl functional group as an integral part of their structure. Progesterone is a hormone secreted by the ovaries. It stimulates the growth of cells in the wall of the uterus, preparing the uterine wall for attachment of the fertilized egg. Testosterone is the main male sex hormone. These (and other) sex hormones affect our development and our lives in most fundamental ways.

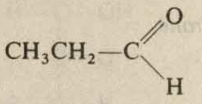
Problems

1. Draw structures and give common and IUPAC names for the four isomeric aldehydes having the formula $C_5H_{10}O$.
2. Draw structures and give common and IUPAC names for the three isomeric ketones having the formula $C_5H_{10}O$.
3. Give suitable names to the following.

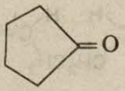
a.



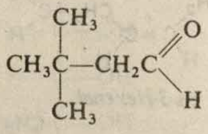
d.



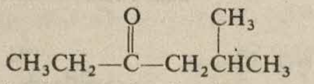
b.



e.



c.



$\mathrm{CH_3CH_2{-}\overset{\overset{O}{\|}}{C}{-}CH_2\overset{\overset{CH_3}{|}}{C}HCH_3}$

4. Write the equation for the reaction of acetaldehyde with each of the following.
   a. water
   b. 1 mole of CH_3OH
   c. 2 moles of CH_3OH, with dry HCl present
   d. phenylhydrazine ($NH_2NHC_6H_5$)
   e. dilute base (aldol condensation)
5. Write the equation for the reaction of acetone with the reagents in problem 4.
6. What reagent would you use to distinguish between 2-pentanone and 2-pentanol? What would be observed when the reagent was added?
7. What reagent would you use to distinguish between acetone and propionaldehyde? What would you observe?
8. Draw the carbanion that would be formed by the action of OH^- on acetone.
9. Write the structure for the enol form of acetone.
10. Which of the compounds in **figure 17.4** would give a positive Tollens test? Which would react with phenylhydrazine to give a phenylhydrazone?
11. Name three aldehydes or ketones which serve as active principles in flavors or aromas.

References and Readings

1. Brown, Ronald F., *Organic Chemistry*, Belmont, Calif.: Wadsworth, 1975. Chapter 16 is very good.
2. Furia, T. E., and Bellanca, Nicoló, eds., *Fenaroli's Handbook of Flavor Ingredients*, Cleveland: Chemical Rubber, 1971.
3. Gutsche, C. David, *The Chemistry of Carbonyl Compounds*, Englewood Cliffs, N.J.: Prentice-Hall, 1967.
4. Labianca, Dominick A., "Drug Interaction and 'Knockout Drops,'" *Journal of Chemical Education*, February 1975, p. 101.
5. Noller, Carl R., *Chemistry of Organic Compounds*, 3rd ed., Philadelphia: W. B. Saunders, 1965. See especially chapters 13 and 27.

chapter 18

Organic Acids and Derivatives

Organic acids were known long before the inorganic acids were isolated. We studied some inorganic acids (HCl and H_2SO_4) first; however, primitive tribes were more familiar with organic acids, such as that obtained when their fermentation reactions went awry and produced not alcohol but vinegar. Naturalists of the 17th century knew that the sting of a red ant's bite was due to an organic acid which that pest injected into the wound. And it was long recognized that the crisp, tart flavor of citrus fruits was produced by an organic compound appropriately called citric acid. The acetic acid of vinegar, the formic acid of red ants, and the citric acid of fruits all belong to the same family of compounds, the carboxylic acids.

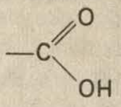
A number of derivatives of carboxylic acids are also important. The amides, of which proteins (chapter 24) are perhaps the most spectacular example, and the esters, which include fats (chapter 23), are two classes of acid derivatives which we shall consider most carefully. Two synthetic fibers (chapter 21) are also classed within these two families of derivatives. Nylon, like silk and wool, is a polyamide. *Dacron*, from which popular "double-knit" pants and other garments are made, is a polyester.

In this chapter we shall look at simple carboxylic acids and at esters and amides, two kinds of acid derivatives. The more complex worlds of proteins and synthetic polymers we shall save for later chapters.

18.1 Acids and Their Derivatives: Functional Groups Galore

We spoke of the carbonyl group in the previous chapter, and we noted that it was this functional group which determined the chemistry of the aldehydes and ketones. The carbonyl group is also incorporated in carboxylic acids and the derivatives of carboxylic acids. However, in these compounds the carbonyl group is only one part of the functional group which characterizes these families.

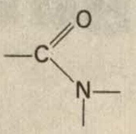
The functional group of the *carboxylic acids* is the *carboxyl* group.



(or —COOH)

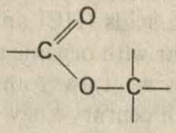
This group can be considered a combination of the carbonyl group (>C=O) and the hydroxyl group (—OH), but it has characteristic properties of its own.

In the *amides* the functional group is



Here we have the carbonyl group attached to a nitrogen. The properties of the amide functional group are different from those of the simple carbonyl group and those of simple nitrogen-containing compounds, called amines (chapter 19).

The functional group of the *esters* looks a little like that of an ether and a little like that of a carboxylic acid.



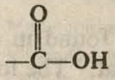
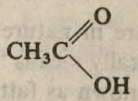
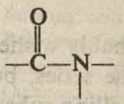
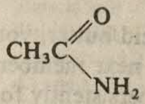
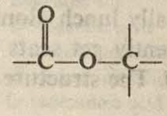
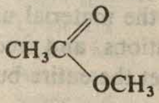
As you should now suspect, compounds incorporating this group react neither like acids nor like ethers, but rather like a distinctive family of compounds.

We keep talking about the derivatives of carboxylic acids. All of the families we shall discuss in this chapter, excluding the carboxylic acids themselves, are regarded as derived from the acid. In each case, the hydroxyl group of the acid's functional group is replaced with some other group in the derivative. **Table 18.1** gathers all of these functional groups in one location to permit you to compare and contrast the various groups more easily. The table also offers an example (with names) for each type of compound. We shall consider nomenclature in more detail as we take up each of these families separately.

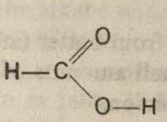
18.2 Some Common Acids: Structures and Names

Most of the organic acids that we will consider are derived from natural sources. These acids have common names, often associated with the natural source, that are widely used. These common names, as we mentioned in the previous chapter, have even been adapted for use with other families of organic compounds, such as the aldehydes. The names of the acid derivatives are also based on the common names of the acids. In many ways, the common nomenclature of carboxylic acids will serve the same basic function as the IUPAC rules for naming alkanes. Once you've learned the common names for the acids, the naming of derivatives will involve only slight modifications of the original acid names.

Table 18.1
Carboxylic acid derivatives

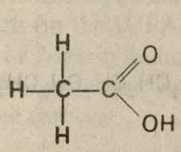
Family	*Functional Group*	*Example*	*Common Name*	*IUPAC Name*
Carboxylic acid	 $-\overset{O}{\overset{\|}{C}}-OH$		Acetic acid	Ethanoic acid
Amide	 $-\overset{O}{\overset{\|}{C}}-\underset{\|}{N}-$		Acetamide	Ethanamide
Ester	 $-\overset{O}{\overset{\|}{C}}-O-\underset{\|}{\overset{\|}{C}}-$		Methyl acetate	Methyl ethanoate

The simplest organic acid is formic acid (from the Latin *formica,* "ant"). It was first obtained by the destructive distillation of ants. The structure of formic acid is



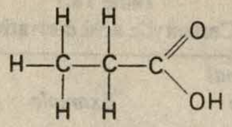
Note that this compound is classed as a carboxylic acid and *not* as an aldehyde. The aldehyde functional group was described as consisting of a carbonyl group with at least one hydrogen attached to the carbon of the carbonyl. The structure of formic acid apparently fits this description. But the carbonyl is also attached to a hydroxyl group and it is this group which determines the nature of the functional group as a whole. To be an aldehyde a compound can have, in addition to the requisite hydrogen, only a carbon or another hydrogen attached to the carbonyl carbon.

Acetic acid, the next member of the series, can be made by the *aerobic* ("with air") fermentation of a mixture of cider and honey. This produces a solution of vinegar which contains about 4% to 10% acetic acid plus a number of other compounds which give the vinegar flavor. The structure of acetic acid is



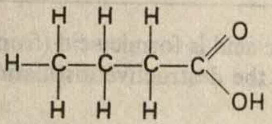
It is probably the most familiar *weak* acid used in educational and industrial chemistry laboratories.

The next compound in the homologous series of aliphatic acids is called propionic acid.



This compound is rather rare in nature. It is found in dairy products in small amounts. Its name literally means "first fat." The longer, continuous-chain carboxylic acids are known as fatty acids because many of them are isolated from natural fats.

If you ever smelled rancid butter, you probably wished you hadn't. But you would know what the next member of the series, butyric acid, smells like. It is one of the most persistently foul smelling substances imaginable. Chemists who work with the material usually lunch alone, are engaged in only the briefest conversations, and frequently get seats on very crowded buses (occasionally they get the entire bus). The structure of butyric acid is

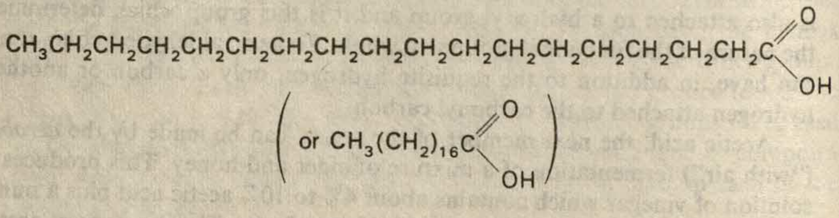


Butyric acid can be isolated from butter fat. It is also one of the ingredients of body odor. Extremely small amounts of this and other chemicals enable the bloodhound to track a person.

I THINK THE OTHER CHEMISTS ARE JEALOUS OF MY WORK ON THE BUTTER FLAVOR, DOCTOR. NO ONE TALKS TO ME ANYMORE.

Figure 18.1 Chemists who work with butyric acid aren't always the most popular people.

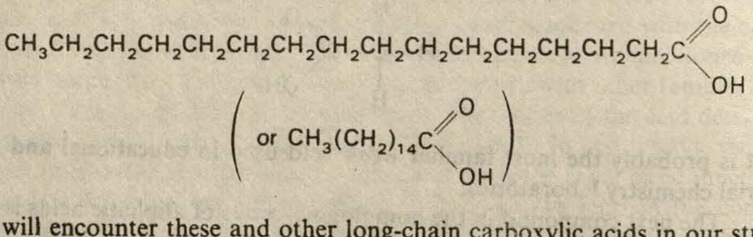
Many other carboxylic acids occur in nature. Let's look at two more examples now. Stearic acid ($C_{18}H_{36}O_2$) is a rather large molecule obtained from fat. Beef tallow is a particularly good source. The structure of stearic acid, in condensed form, is



$$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2C(=O)OH$$

$$\left(\text{or } CH_3(CH_2)_{16}C(=O)OH\right)$$

Palmitic acid ($C_{16}H_{32}O_2$) is obtained from coconut oil. Its structure, condensed, is



$$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2C(=O)OH$$

$$\left(\text{or } CH_3(CH_2)_{14}C(=O)OH\right)$$

We will encounter these and other long-chain carboxylic acids in our study of fats (chapter 23).

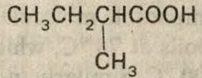
Table 18.2
Names of some common aliphatic acids

Condensed Formula	*IUPAC Name*	*Common Name*	*Derivation of Common Name*
HCOOH	Methanoic acid	Formic acid	Latin *formica*, "ant"
CH_3COOH	Ethanoic acid	Acetic acid	Latin *acetum*, "vinegar"
CH_3CH_2COOH	Propanoic acid	Propionic acid	Greek *protos*, "first," and *pion*, "fat"
$CH_3CH_2CH_2COOH$	Butanoic acid	Butyric acid	Latin *butyrum*, "butter"
$CH_3(CH_2)_3COOH$	Pentanoic acid	Valeric acid	Latin *valere*, "powerful"
$CH_3(CH_2)_4COOH$	Hexanoic acid	Caproic acid	Latin *caper*, "goat"
$CH_3(CH_2)_6COOH$	Octanoic acid	Caprylic acid	
$CH_3(CH_2)_8COOH$	Decanoic acid	Capric acid	
$CH_3(CH_2)_{10}COOH$	Dodecanoic acid	Lauric acid	Laurel tree
$CH_3(CH_2)_{12}COOH$	Tetradecanoic acid	Myristic acid	*Myristica fragrans* (nutmeg)
$CH_3(CH_2)_{14}COOH$	Hexadecanoic acid	Palmitic acid	Palm tree
$CH_3(CH_2)_{16}COOH$	Octadecanoic acid	Stearic acid	Greek *stear*, "tallow"

Although IUPAC names are seldom encountered in everyday use, they are readily derived from the names of alkanes with the same number of carbon atoms. Just drop the *-e* from the alkane name and add *-oic acid*. Thus, the IUPAC name for formic acid (H—COOH, or CH_2O_2) is methanoic acid and that for acetic acid (CH_3COOH) is ethanoic acid. The names of several common aliphatic acids are shown in **table 18.2.** Nature prefers an even number of carbon atoms in its acids. Therefore, beyond six carbon atoms, we have listed only the commonly isolated, even-numbered acids.

If substituents are attached to the parent chain of the acid, the rules outlined in section 17.2 are applied. Greek letters are used with common names; numbers are used with IUPAC names. The carbon of the carboxyl group is always considered the first carbon.

Example 18.1 Give the common and IUPAC names for

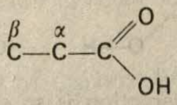


$$CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCOOH$$

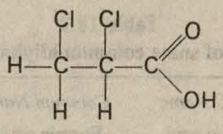
The longest continuous chain contains four carbon atoms; the compound is therefore named as a substituted butyric (or butanoic) acid. The methyl substituent is at the alpha carbon (in the common system), or at the second carbon (in the IUPAC system). The compound is α-methylbutyric acid, or 2-methylbutanoic acid.

Example 18.2 Draw α, β-dichloropropionic acid.

Propionic acid contains three carbons.



Two chlorine atoms must be attached to the parent chain, one at the alpha carbon and one at the beta carbon.



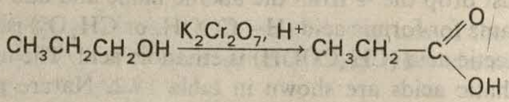
The simplest aromatic acid is called benzoic acid. Others are called by common names or may be named as derivatives of benzoic acid.

A number of dicarboxylic acids, both aliphatic and aromatic, are worthy of mention. Seven of these are given, with names, in **table 18.3.**

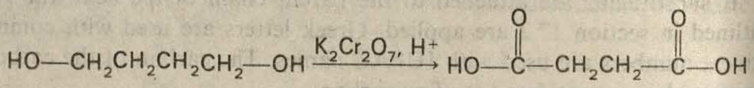
18.3 Carboxylic Acids: Preparation and Physical Properties

Few carboxylic acids occur free in nature. Many aliphatic acids, particularly those with an even number of carbon atoms, are found combined with glycerol in fats (chapter 23). Some of the acids are thus available from the hydrolysis of fats.

A general method for the preparation of carboxylic acids is by the oxidation of primary alcohols (chapter 16). For example, *n*-propyl alcohol can be oxidized, by an acidic solution of potassium dichromate, to propionic acid.



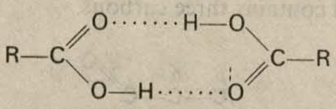
In a similar manner, 1,4-butanediol is oxidized to succinic acid.



$$HO{-}CH_2CH_2CH_2CH_2{-}OH \xrightarrow{K_2Cr_2O_7,\ H^+} HO{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_2CH_2{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OH$$

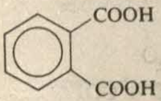
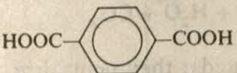
Carboxylic acids are highly polar and exhibit strong intermolecular hydrogen bonding. Consequently, these compounds have higher boiling points than even the alcohols of comparable molecular weights. Ethyl alcohol (with a molecular weight of 46) boils at 78 °C, while formic acid (with the same molecular weight) boils at 100 °C. Similarly, *n*-propyl alcohol (with a molecular weight of 60) boils at 97 °C, while acetic acid (with the same molecular weight) boils at 118 °C.

There is good evidence that, even in the vapor phase, some of the hydrogen bonds between acid molecules are not broken. The particular structure of the carboxyl group permits two molecules to hydrogen bond very strongly to one another.



In many situations, the interaction is so strong that the *dimer* (the two-molecule unit) acts as a single particle. Osmotic pressures, freezing-point depressions, and other properties are frequently lower than one would ex-

Table 18.3
Some common dicarboxylic acids

Structure	*IUPAC Name*	*Common Name*	*Derivation of Common Name*
HOOC—COOH	Ethanedioc acid	Oxalic acid	Greek *oxys*, "sharp" or "acid"
HOOC—CH_2—COOH	Propanedioc acid	Malonic acid	From malic acid (Latin *malum*, "apple")
$HOOC(CH_2)_2COOH$	Butanedioc acid	Succinic acid	Latin *succinum*, "amber"
$HOOC(CH_2)_3COOH$	Pentanedioc acid	Glutaric acid	From glutamic acid (Latin *gluten*, "glue")
$HOOC(CH_2)_4COOH$	Hexanedioc acid	Adipic acid	Latin *adeps*, "fat"
	1,2-Benzenedicarboxylic acid	Phthalic acid	From na*phthal*ene
	1,4-Benzenedicarboxylic acid	Terephthalic acid	From na*phthal*ene

pect when carboxylic acids are the solute. That is because we are counting as two separate molecules a combination which is behaving as one piece.

The carboxyl groups readily hydrogen bond to water molecules. The acids having one to four carbon atoms are colorless liquids which are completely miscible with water. Solubility decreases with increasing number of carbons. Hexanoic acid ($C_6H_{12}O_2$) is soluble only to the extent of 1.0 g per 100 g of water. Palmitic acid ($C_{16}H_{32}O_2$) is essentially insoluble.

Most of the carboxylic acids have irritating, obnoxious odors. Generally, the odors get more unpleasant as one goes up the homologous series, depending, of course, on how one defines unpleasant. Formic acid (CH_2O_2) has a very sharp and penetrating odor. Valeric acid ($C_5H_{10}O_2$) is not quite so aggressive, but it is nonetheless quite bad. It is most gently described as clinging or persistent and far more descriptively pinpointed as "essence of old gym sneakers." This trend in odors is alleviated somewhat by the decreasing tendency of the acids to vaporize as molecular weight increases. For acids with 12 or more carbons, odors become progressively weaker.

Pure acetic acid freezes at 16.6 °C (62 °F). Since this is only slightly below normal room temperature (about 20 °C, or 68 °F), acetic acid solidifies when cooled only slightly. In the poorly heated laboratories of a century or so ago in northern North America and Europe, acetic acid often froze on the reagent shelf. For that reason, pure acetic acid (sometimes referred to as concentrated acetic acid) came to be known as glacial acetic acid, a name which survives to this day.

18.4 Chemical Properties of Carboxylic Acids: Acids Are Acids

In chapter 10 we defined an acid as a compound which (1) turns blue litmus red, (2) neutralizes bases, (3) reacts with active metals to give off hydrogen, and (4) tastes sour. Of the four properties of acids listed, you are probably most familiar with the last—sour taste. Vinegar is sour because it contains acetic acid. Grapefruits and lemons are sour because they contain citric acid. Sour milk contains lactic acid. The acids we eat are, for the most part, organic acids. The strong acids that we encountered in chapter 10, such as hydrochloric acid (HCl), nitric acid (HNO_3), and sulfuric acid (H_2SO_4), are made from minerals and hence are called *mineral acids*. Historically, the first organic acids came from plant or animal matter, that is, from organisms. Now, many organic acids are synthesized in the laboratory from coal tar or petroleum products.

Those carboxylic acids that are water soluble form moderately acidic solutions. They will change litmus from blue to red. Carboxylic acids, whether water soluble or not, will react with aqueous solutions of sodium hydroxide, sodium carbonate, and sodium bicarbonate to form salts.

$$R{-}COOH + NaOH(aq) \longrightarrow R{-}COO^-Na^+(aq) + H_2O$$

$$2\ R{-}COOH + Na_2CO_3(aq) \longrightarrow 2\ R{-}COO^-Na^+(aq) + H_2O + CO_2$$

$$R{-}COOH + NaHCO_3(aq) \longrightarrow R{-}COO^-Na^+(aq) + H_2O + CO_2$$

In these reactions, the carboxylic acids act as typical acids; they neutralize basic compounds. With solutions of carbonate and bicarbonate ions they also form carbon dioxide gas.

The carboxylic acids are weak acids. They tend to ionize only slightly in aqueous solution.

$$R{-}COOH + H_2O \longrightarrow R{-}COO^- + H_3O^+$$

Acetic acid was one of the weak acids listed in chapter 10. The time has now come for us to distinguish between degrees of weakness. We can order some organic compounds (and some inorganic ones) according to their relative acidities.

Strongest acid *Weakest acid*

H_2SO_4, HNO_3, HCl >	$R{-}COOH$ >	H_2CO_3 >	$ArOH$ >	H_2O >	ROH >	RH
Mineral acids	*Carboxylic acids*	*Carbonic acid*	*Phenols*	*Water*	*Alcohols*	*Alkanes*

Water is frequently used as a dividing line for acidity and basicity. Because we live in a water world, we quite naturally regard water as neutral. If something is more acidic than water, it is treated as an acid (as are phenols and carboxylic acids). If a compound is less acidic than water (as are alcohols and alkanes), it is not regarded as an acid. Another critical dividing line is that established by carbonic acid. In *organic* chemistry, a compound which is more acidic than carbonic acid is occasionally referred to as a "strong" acid. Those compounds weaker than carbonic acid but still stronger than water are called "weak" acids. Thus, carboxylic acids are frequently called "strong" acids by organic chemists, while phenols are referred to as "weak" acids. It is important to realize that both carboxylic acids and phenols should

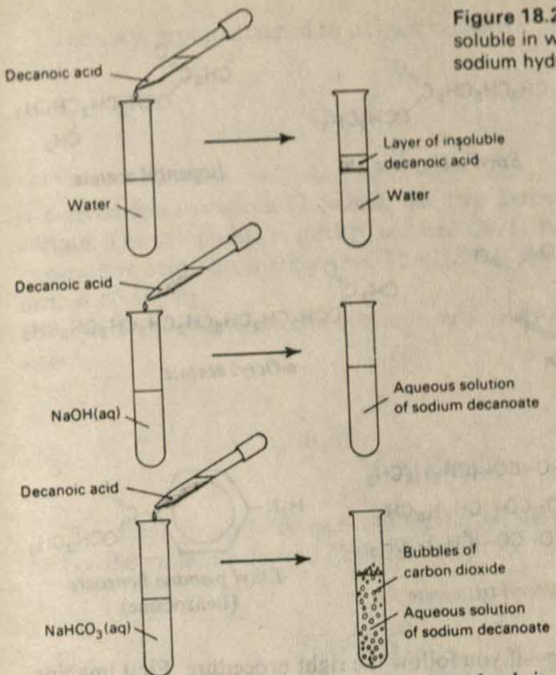
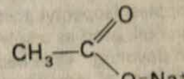


Figure 18.2 Decanoic acid is insoluble in water but soluble in aqueous sodium hydroxide or bicarbonate.

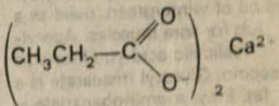
accurately be classified as weak acids since both ionize only slightly in water solutions. When organic chemists speak of acetic acid as a strong acid, they really mean it is stronger than phenol. Compared to hydrochloric or sulfuric acid, acetic acid is a very weak acid indeed.

Because of the difference in relative acidities among organic compounds, solubility behavior is often an identifying feature of carboxylic acids. Carboxylic acids which are insoluble in water dissolve in aqueous hydroxide, carbonate, or bicarbonate because the insoluble acids react to form ionic salts which are water soluble. The behavior of decanoic acid is illustrated in **figure 18.2.** Solution in aqueous bicarbonate, with the formation of carbon dioxide bubbles, is characteristic of carboxylic acids.

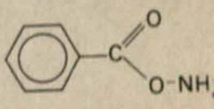
The relationship between the names of acids and their corresponding anions was discussed in section 10.3. The naming of salts in general was first encountered in section 4.6. You have been working with the salt of at least one organic acid for quite a while—sodium acetate or, more generally, the acetate ion. To name the salts of carboxylic acids, simply name the cation first and then name the anion by changing the *-ic* ending of the acid to *-ate.*



Sodium acetate
(sodium ethanoate)



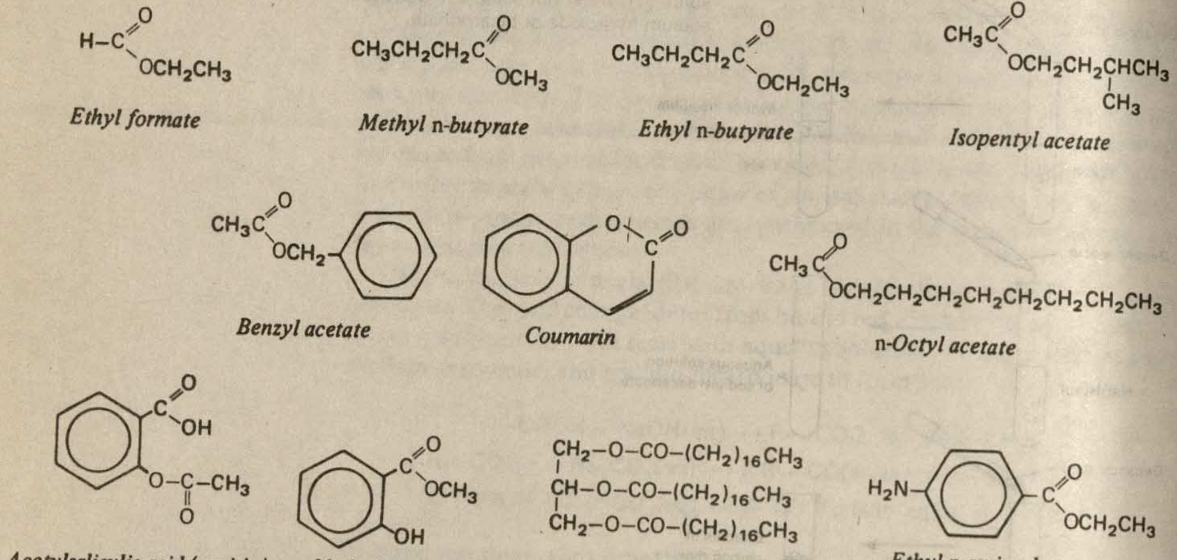
Calcium propionate
(calcium propanoate)



Ammonium benzoate

18.5 An Ester by Any Other Name . . .

Esters generally have pleasant odors and are often responsible for the characteristic fragrances of fruits and flowers. Once a flower or fruit has been chemically analyzed, flavor chemists can attempt to duplicate the natural odor or taste. They are seldom completely successful, but they often get close enough for practical purposes. Artificial fruit flavors are often mixtures of esters. Several esters of interest are shown in **figure 18.3.**



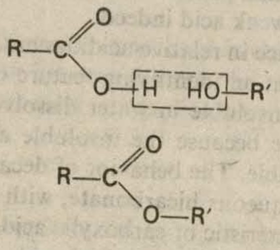
Ethyl formate *Methyl* n-*butyrate* *Ethyl* n-*butyrate* *Isopentyl acetate*

Benzyl acetate *Coumarin* n-*Octyl acetate*

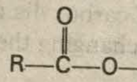
Acetylsalicylic acid (aspirin) *Methyl salicylate* *Glyceryl tristearate* *Ethyl* p-*amino benzoate* (Benzocaine)

Figure 18.3 Some esters of interest. Ethyl formate is an artificial rum flavor. Methyl *n*-butyrate occurs in apples, and ethyl *n*-butyrate occurs in pineapples. Isopentyl acetate is banana oil, used as a solvent and in flavoring, while benzyl acetate is oil of jasmine, used in perfumes. Coumarin is responsible for the odor in new-mown hay and sweet-clover. *n*-Octyl acetate occurs in oranges. Methyl salicylate is oil of wintergreen, used as a rub for sore muscles. Acetylsalicylic acid you know as aspirin. Glyceryl tristearate is a fat. Ethyl *p*-aminobenzoate is used as a local anesthetic.

Esters are easy to name—if you follow the right procedure. First imagine the ester to have been made from an acid and an alcohol through the loss of water.



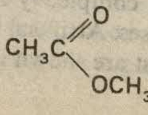
Then name the alkyl group from the alcohol, designated R′ in the formula. (Notice that the alkyl group from the alcohol is attached directly to an oxygen by a single bond.) Finally, name the part derived from the acid,



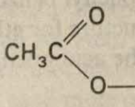
$$\overset{\displaystyle O}{\overset{\|}{R—C—O—}}$$

as if it were an anion (section 18.4).

Example 18.3 What are the common and IUPAC names for this ester?

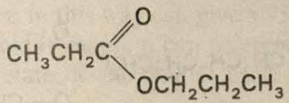


The alkyl group attached to oxygen is methyl. The

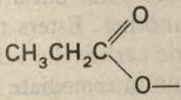


is derived from acetic acid (which has two carbons). Its name is acetate. The compound is methyl acetate. The IUPAC name for the two-carbon acid unit is ethanoate. The IUPAC name for the ester is methyl ethanoate.

Example 18.4 What are the common and IUPAC names for this ester?

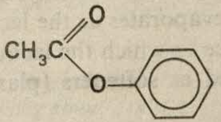


The alkyl group (attached directly to oxygen) is *n*-propyl. The part of the molecule derived from the acid,



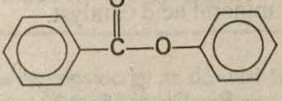
has three carbon atoms. It is thus called propionate, or, by IUPAC terminology, propanoate. The common name of the ester is, therefore, *n*-propyl propionate, and the IUPAC name is propyl propanoate.

Esters of phenol are named as *phenyl,** followed by the name of the anion of the acid. The compound



is phenyl acetate.

Example 18.5 What is the name of this ester?



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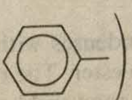
*Phenyl is C_6H_5— (or

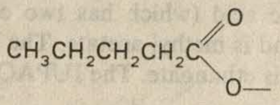


)

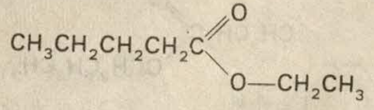
The group attached by a single bond to oxygen is phenyl. The acid portion corresponds to the benzoate group (from benzoic acid). Therefore, the compound is phenyl benzoate.

Example 18.6 Draw the structure for ethyl valerate.

It is easier to start with the acid portion. Draw the valerate (five-carbon) group first.

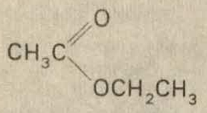


Then simply attach the ethyl group to the bond which ordinarily holds the hydrogen in the free acid.

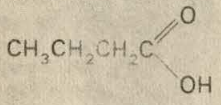


18.6 Physical Properties of the Esters

The molecules of an ester are polar but are incapable of intermolecular hydrogen bonding with one another. Esters thus have considerably lower boiling points than the isomeric carboxylic acids. As one might expect, the boiling points of esters are about intermediate between those of ketones and ethers of comparable molecular weight.



Ethyl acetate ($C_4H_8O_2$)
(boiling point, 77 °C)



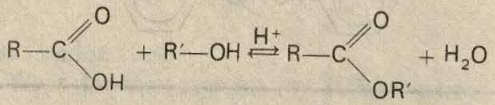
Butyric acid ($C_4H_8O_2$)
(boiling point, 164 °C)

Ester molecules are capable of hydrogen bonding to water molecules, rendering esters of low molecular weight somewhat water soluble. Borderline solubility occurs in those molecules having from three to five carbon atoms.

Esters dissolve many organic substances. They are often employed as solvents. Cellulose nitrate is dissolved in ethyl acetate and butyl acetates to form lacquers. The solvent evaporates as the lacquer "dries," leaving a thin protective film on the surface to which the lacquer was applied. Esters with high boiling points are used as softeners (plasticizers) for brittle plastics (chapter 21).

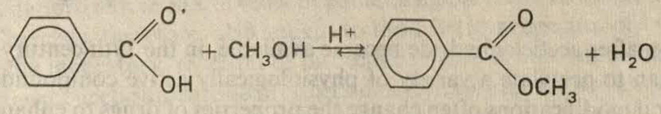
18.7 Preparation of Esters: Aspirin and Heroin

Some esters are prepared by direct esterification of the carboxylic acid. This is accomplished through the heating of a carboxylic acid with an alcohol in the presence of a mineral acid catalyst.



An alcohol molecule condenses with an acid molecule, splitting out water (dehydrating) to form an ester. The reaction is reversible, and it soon comes to equilibrium. To get a good yield of ester, it is necessary to apply a stress to the system, forcing the reaction to the right (a technique that was discussed in chapter 5).

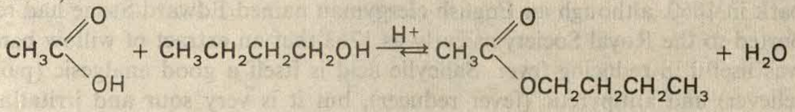
If the reaction involves an inexpensive alcohol, such as methanol (CH_3OH), excess alcohol can be used. This will drive the reaction toward completion. In the preparation of methyl benzoate, for example, 10 moles of CH_3OH may be used for each mole of benzoic acid.



(Large excess)

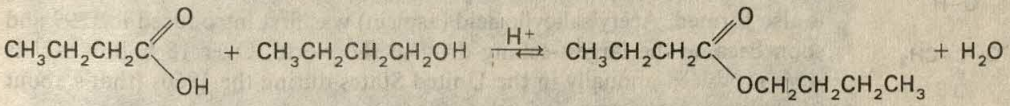
Forcing of the reaction in this way can give a 75% yield of methyl benzoate.

Similarly, if the acid is cheap, it can be employed in excess. In the preparation of *n*-butyl acetate, acetic acid is used in a molar ratio of 2:1 (or greater).



(Excess)

A third method of driving the reaction toward completion involves removal of the product water as it is formed. This is easily accomplished if the acid, the alcohol, and the ester all boil at temperatures of well above 100 °C.



Butyric acid (boiling point, 164 °C)

Butyl alcohol (boiling point, 118 °C)

Butyl butyrate (boiling point, 165 °C)

Distilled from mixture (boiling point, 100 °C)

Esters of acetic acid are usually prepared by use of *acetic anhydride.** *n*-Octyl acetate can be made from octyl alcohol.

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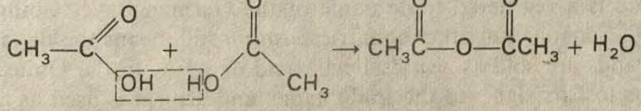
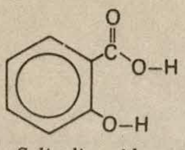
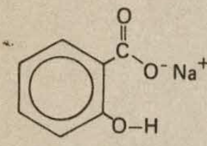
*Acetic anhydride can be considered as derived from acetic acid by the removal of one molecule of water from two molecules of acid.

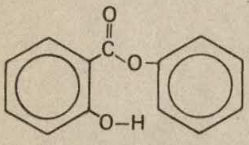




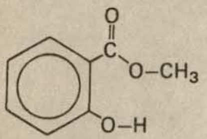
Salicylic acid



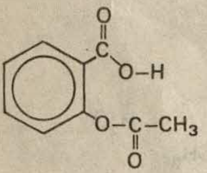
Sodium salicylate



Phenyl salicylate (salol)

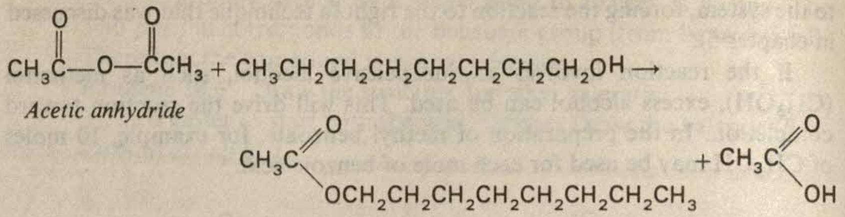


Methyl salicylate



Acetylsalicylic acid

Figure 18.4 Salicylic acid and some of its derivatives.



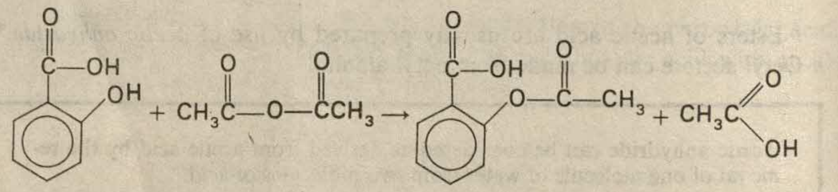
Acetic anhydride

Soon after acetic anhydride became available, in the 19th century, chemists began to acetylate a variety of physiologically active compounds. Such structural modifications often change the properties of drugs to enhance their effectiveness or to minimize undesirable side effects. Two such cases will be described here, that of aspirin and that of heroin.

People have long sought relief from pain. Alcohol, opium, cocaine, and Indian hemp (marijuana) were used as medicines for relief of pain in some early societies. The first successful synthetic pain relievers were derivatives of salicylic acid (**figure 18.4**). Salicylic acid was first isolated from willow bark in 1860, although an English clergyman named Edward Stone had reported to the Royal Society as early as 1763 that an extract of willow bark was useful in reducing fever. Salicylic acid is itself a good analgesic (pain reliever) and antipyretic (fever reducer), but it is very sour and irritating when taken by mouth. Chemists sought to modify the structure of the molecule to remove this undesirable property while retaining (or even improving) the desirable properties.

Sodium salicylate was first used in 1875. It was less unpleasant when taken by mouth than salicylic acid but proved to be highly irritating to the lining of the stomach. Phenyl salicylate (salol) was introduced in 1886. It passes unchanged through the stomach. In the small intestine it is hydrolyzed (section 18.8) to the desired salicylic acid, but phenol, which is rather toxic, is also formed. Acetylsalicylic acid (aspirin) was first introduced in 1899 and soon became the largest-selling drug in the world. Over 15 billion tablets were produced annually in the United States during the 1960s (that's about 75 tablets for every person in the country).

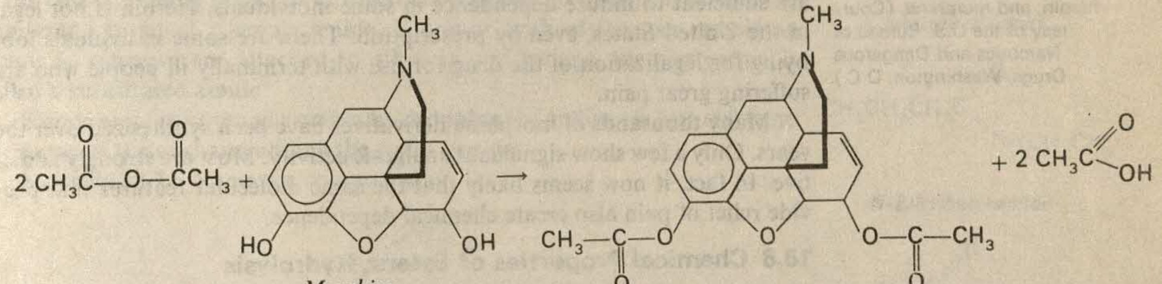
Acetylsalicylic acid is made by treatment of salicylic acid with acetic anhydride. In this reaction, the hydroxyl group of the phenol reacts exactly like that of an alcohol.



Aspirin is a registered trade name of the German Bayer Company. In Germany, Canada, and other countries, *aspirin* still means the Bayer brand. Other brands are sold as acetylsalicylic acid or ASA. In the United States, Bayer has lost its rights to the trade name, and aspirin is used as a generic name for acetylsalicylic acid. Aspirin is a chemical compound, and, as with other compounds, its properties are invariant. Aspirin *tablets* usually contain 324 mg (5 grains) each of this compound, held together with some sort of inert binder. The latter may be starch, clay, or a sugar. Various brands of aspirin have been extensively tested. The conclusions of impartial studies are invariably the same: the only significant difference in brands is price.

Morphine, an opium alkaloid, is a *narcotic,* that is, a drug which produces both sedation (narcosis) and relief of pain (analgesia). It is also strongly addictive. Chemists, therefore, also sought to modify the properties of morphine.

In the laboratory, reaction of morphine (which is both an alcohol and a phenol) with acetic anhydride produces diacetylmorphine, a product in which both the alcohol and phenol hydroxyl groups have been esterified.



Morphine

Heroin
(diacetylmorphine)

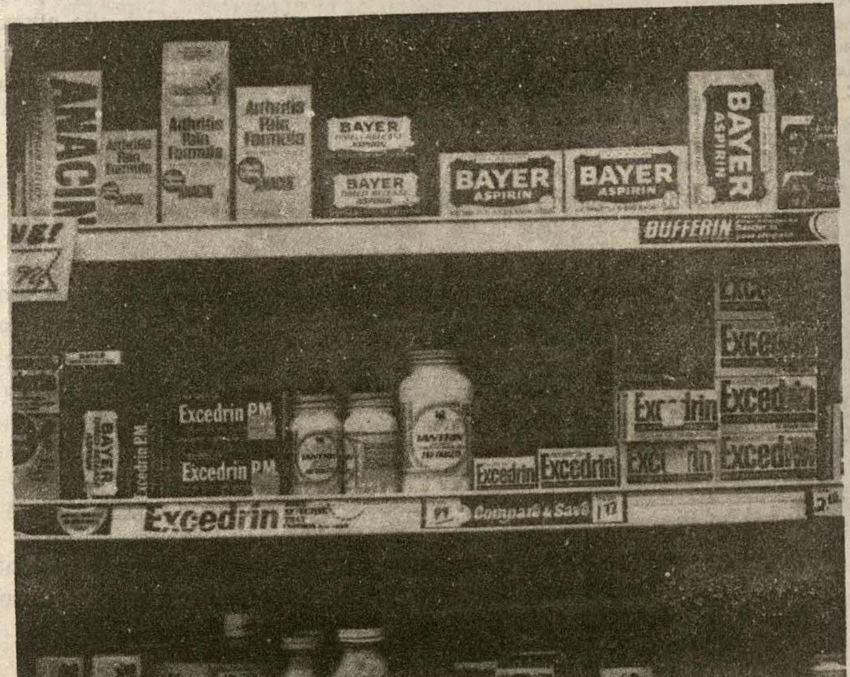


Figure 18.5 Pain relievers readily available to the public. (Photo by Dennis Tasa.)

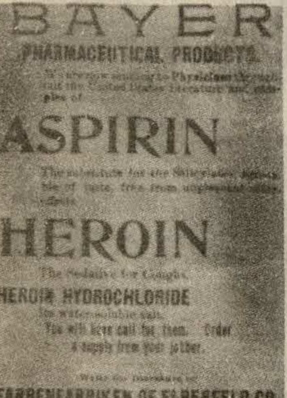
Figure 18.6 Opium poppy and derivatives, crude and smoking opium, codeine, heroin, and morphine. (Courtesy of the U.S. Bureau of Narcotics and Dangerous Drugs, Washington, D.C.)

This morphine derivative was first prepared by chemists at the Bayer Company of Germany in 1874. Indeed, the name *heroin* is Bayer's trade name for diacetylmorphine. Heroin received little attention until 1890, when it was proposed as an antidote for morphine addiction! Shortly thereafter, Bayer was widely advertising heroin as a sedative for coughs, often in the same advertisement with aspirin (**figure 18.7**). However, it was soon found that heroin induced addiction more quickly than morphine and that heroin addiction was harder to cure.

The physiological action of heroin is similar to that of morphine except that heroin produces a stronger feeling of euphoria for a longer period of time. Heroin is so strongly addictive that it seems that one or two injections are sufficient to induce dependence in some individuals. Heroin is not legal in the United States, even by prescription. There are some individuals lobbying for legalization of the drug for use with terminally ill people who are suffering great pain.

Many thousands of morphine derivatives have been synthesized over the years. Only a few show significant analgesic activity. Most are strongly addictive. In fact, it now seems likely that the same molecular features that provide relief of pain also create chemical dependence.

Figure 18.7 Heroin advocated as a safe medicine in 1900. It was widely marketed as a sedative for coughs. (Courtesy of the U.S. Bureau of Narcotics and Dangerous Drugs, Washington, D.C.)



BAYER

PHARMACEUTICAL PRODUCTS

ASPIRIN

HEROIN

The Sedative for Coughs

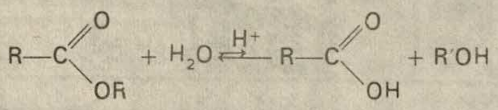
HEROIN HYDROCHLORIDE

FARBENFABRIKEN OF ELBERFELD CO.

40 Stone Street, New York.

18.8 Chemical Properties of Esters: Hydrolysis

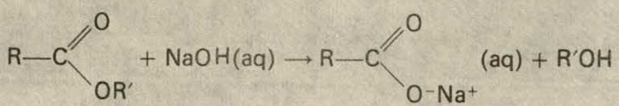
Esters are neutral compounds, unlike the acids from which they are formed. As neutral compounds they exhibit neither acidic nor basic properties. Esters typically undergo chemical reactions in which the alkoxy (—OR′) group is replaced by another group. One such reaction is hydrolysis, or splitting with water. Hydrolysis is catalyzed by either acid or base. Acidic hydrolysis is simply the reverse of the esterification reaction (p. 386).



$$R{-}C(=O){-}OR + H_2O \overset{H^+}{\rightleftharpoons} R{-}C(=O){-}OH + R'OH$$

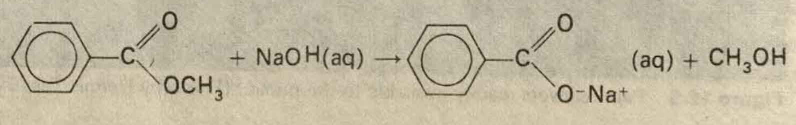
As in esterification, the reaction comes to equilibrium, and the position of the equilibrium can be shifted by addition or removal of one or another of the species involved.

Basic or alkaline hydrolysis, on the other hand, goes to completion.



$$R{-}C(=O){-}OR' + NaOH(aq) \rightarrow R{-}C(=O){-}O^-Na^+(aq) + R'OH$$

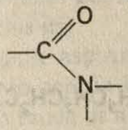
The free acid is not obtained in this reaction. In a basic solution, the salt of the acid is always isolated. Treatment of methyl benzoate with aqueous sodium hydroxide gives sodium benzoate and methyl alcohol.

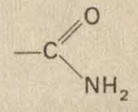


Alkaline hydrolysis of fats and oils (esters of glycerol with long-chain carboxylic acids) is called saponification (from the Latin *sapon*, "soap"). The sodium salts of such fatty acids are soaps (chapter 23).

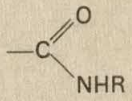
18.9 Amides: Structures and Names

In the amide functional group, a nitrogen is attached to a carbonyl group.





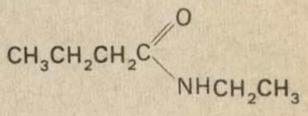
A simple amide



A substituted amide

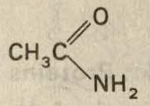
If the two remaining bonds to nitrogen are attached to hydrogen atoms, the compound is called a simple amide. If one or both of the two remaining bonds to nitrogen are attached to alkyl or aryl groups, the compound is called a substituted amide.

Simple amides form their names by dropping the ending *-ic* (or *-oic*) from the name of the acid and adding the suffix *-amide*.

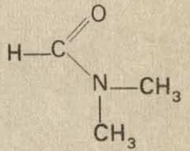


N-Ethylbutyramide

Example 18.7 Name the compound

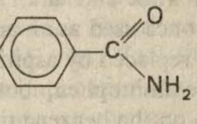


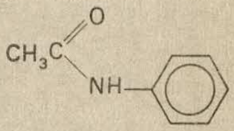
This amide is derived from acetic acid. Drop the *-ic* suffix, attach the ending *-amide*, and you have the name—acetamide (or ethanamide in the IUPAC system).



N,N-Dimethylformamide

Example 18.8 Name the compound



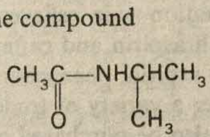


Acetanilide

This amide is derived from benzoic acid. Drop the *-oic*, add *-amide*, and you have it—benzamide.

In substituted amides, alkyl groups attached to the nitrogen atom are named as substituents. Instead of using a Greek letter or a number to specify location, chemists indicate the group's attachment to nitrogen by a capital letter *N*. If the substituent on nitrogen is phenyl, the compound is named as an anilide. The *-ic* or *-oic* ending of the acid name is replaced with *-anilide* instead of *-amide*.

Example 18.9 Name the compound

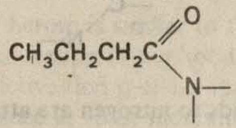


$$\mathrm{CH_3\underset{\underset{O}{\|}}{C}{-}NH\underset{\underset{CH_3}{|}}{C}HCH_3}$$

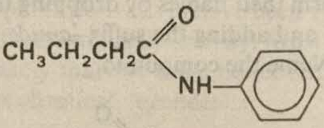
The acid portion of the molecule (the portion incorporating the carbonyl group and to one side of the nitrogen) contains two carbon atoms and is derived from acetic acid. The compound will, therefore, be named as a substituted acetamide. The substituent attached directly to the nitrogen is an isopropyl group. The name of the compound is N-isopropylacetamide. (The IUPAC name is N-isopropylethanamide.)

Example 18.10 Draw butyranilide.

The compound is a substituted four-carbon amide (derived from butyric acid).



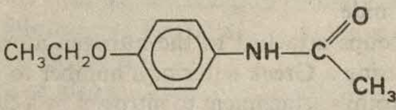
The suffix *-anilide* indicates that there is a phenyl group substituted for one of the two hydrogens on the nitrogen of the simple amide.



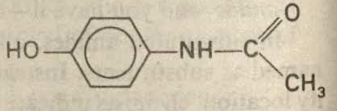
18.10 Amides and People: Proteins and Pain Relievers

The amide functional group is of utmost importance in the chemistry of life. Proteins (chapter 24) are polyamides. If you wish to select a particular type of molecule as the basis of life, the protein is about as close as you can come.

Nylon is a synthetic polyamide, a conscious imitation of the protein structure of the natural fibers wool and silk. Many drugs contain the amide function. Acetanilide was once used as an antipyretic. It is quite toxic, however, and has been largely replaced by aspirin and by two of its own derivatives, phenacetin and acetaminophen, both of which are derived from acetanilide by substitution on the benzene ring.



Phenacetin
(p-*ethoxyacetanilide)*

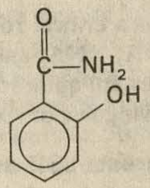


Acetaminophen
(p-*hydroxyacetanilide)*

The so-called combination pain relievers often contain phenacetin or acetaminophen along with aspirin and caffeine. For many years, the most familiar combination was aspirin, phenacetin, and caffeine. This APC combination is available under a variety of trade names, such as *Empirin, Sal-Fayne,* and *PAC*. It can also be purchased as APC Tablets U.S.P., usually at a lower price than the proprietary medications. Phenacetin has about the same effectiveness as aspirin in reducing fever and relieving minor aches and pains. It has been implicated in damage to the kidneys and in blood abnormalities. Perhaps because of these possible side effects, phenacetin has been dropped from *Anacin* and *Excedrin. Anacin,* formerly an APC formulation, now contains only aspirin and caffeine. Caffeine is a mild stimulant found in coffee, tea, and cola syrup. There does not appear to be any reliable evidence that caffeine enhances the effect of aspirin in any significant way. In fact, recent evidence indicates that for fever reduction, caffeine counteracts the action of aspirin. Combinations containing caffeine are therefore *less effective* than plain aspirin for this use.

Some people who are allergic to aspirin may safely take acetaminophen. This compound is comparable to aspirin in relief of pain and reduction of fever. It costs about 10 times as much as aspirin, however. It is available by itself under such trade names as *Tylenol, Tempera, Nebs, Apamide, Lyteca,* and *Datril.*

In *Excedrin,* acetaminophen has replaced the phenacetin which was dropped from the original formulation. This highly advertised product also contains aspirin, salicylamide, and caffeine. Salicylamide, as the name indicates, is the amide of salicylic acid.



Tests have shown this compound to be only half as effective as aspirin for the relief of pain. The advertising claim was made that *Excedrin* is more effective than plain aspirin for pain other than headache. The claim failed to mention that the pain for which *Excedrin* is more effective is that suffered by women who have just had babies! Now, the relief of such pain is certainly a noble undertaking, but the implication that the effect is a general one might be regarded as somewhat more self-serving.

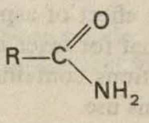
Vanquish, advertised as being "strong medicine," contains aspirin (227 mg), acetaminophen (194 mg), and caffeine (33 mg). The two "gentle buffers" are merely the bases aluminum hydroxide [$Al(OH)_3$] and magnesium hydroxide [$Mg(OH)_2$].

Cope is advertised as a "unique formula for relief of nervous tension headaches." It contains aspirin (421 mg), caffeine (32 mg), and methapyrilene fumarate, as well as magnesium hydroxide and aluminum hydroxide. Methapyrilene fumarate is an *antihistamine!* It does have the side effect of making one drowsy, but just how it helps one "cope" remains a mystery.

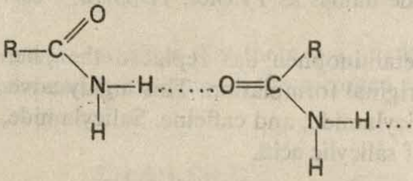
To summarize, extensive studies have shown that of all the preparations on the market, plain aspirin is the cheapest, safest, and most effective for most people. Over-the-counter drugs must list their ingredients on the label. A concerned consumer can easily look up the properties—such as use, toxicity, and side effects—of these ingredients in a reference book such as *The Merck Index.*

18.11 Physical Properties of the Amides

With the exception of the simplest amide (formamide, whose melting point is 3 °C), the amides of the type



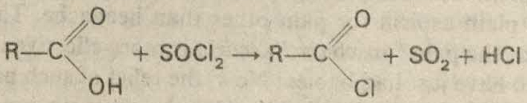
are solids at room temperature. These amides have both relatively high melting points and high boiling points because of strong intermolecular hydrogen bonding.



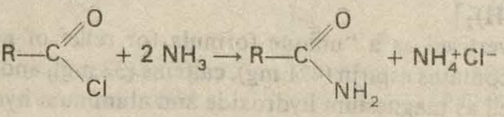
Similar hydrogen bonding plays a critical role in determining the structure and properties of proteins, DNA, RNA, and other giant molecules so important to life processes. Amides are quite soluble in water, with borderline solubility occurring in those having five or six carbon atoms.

18.12 Some Amides of Interest: LSD and Vitamin B_3

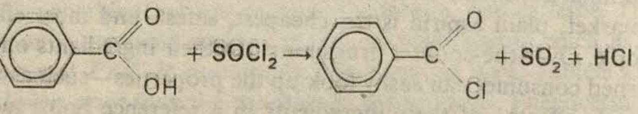
Amides are usually prepared from acids by a two-step process. First the acid is treated with thionyl chloride, converting the former to an acid chloride.



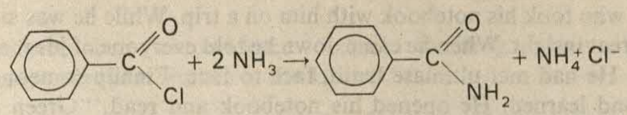
Then the acid chloride is treated with ammonia, and the amide is formed.



To make benzamide, for example, one could first treat benzoic acid with thionyl chloride.

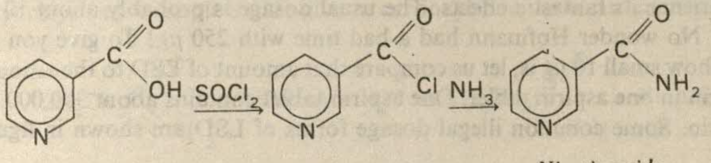


The resulting benzoyl chloride can then react with ammonia, giving benzamide.



The reaction of the acid chloride with ammonia produces both an amide molecule and a molecule of hydrochloric acid, which immediately reacts with more ammonia to form the salt ammonium chloride (NH_4Cl).

Similarly, nicotinamide can be made from nicotinic acid



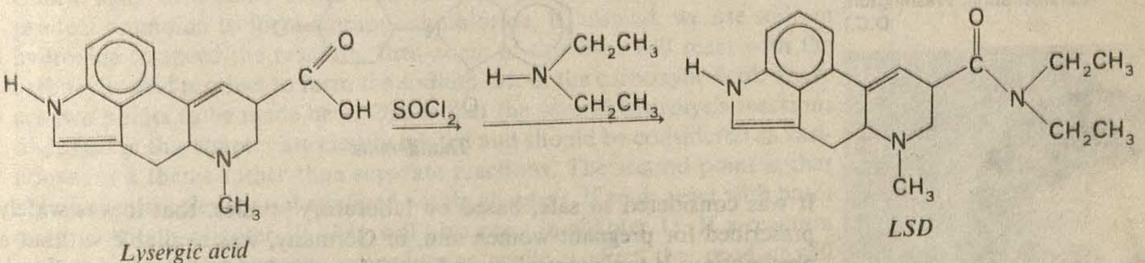
Nicotinic acid (niacin)

Nicotinamide (niacinamide)

Nicotinic acid and nicotinamide (sometimes called vitamin B_3) are essential B vitamins having antipellagra activity (chapter 27).

One of the most interesting amides of all is the N,N-diethylamide of lysergic acid, better known as LSD (from the German *lysergsaure diethylamid*). The physiological properties of this compound were discovered quite accidentally by Albert Hofmann in 1943. Hofmann, a chemist at the Sandoz Laboratories in Switzerland, unintentionally ingested some LSD. He later took 250 μg, which he considered a small dose, to verify that LSD had caused the symptoms he had experienced. Dr. Hofmann had a very rough time for the next few hours, exhibiting such symptoms as visual disturbance and schizophrenic behavior.

Lysergic acid is obtained from ergot, a fungus that grows on rye. It can be converted chemically into LSD by treatment first with thionyl chloride and then with a compound called diethylamine.

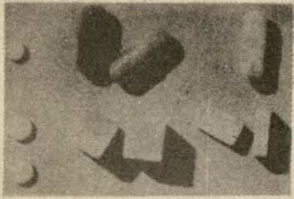


Lysergic acid

LSD

LSD is a member of a class of drugs which qualitatively change the way in which we perceive things. These drugs are called hallucinogenic, psychotomimetic, or psychedelic drugs, because they induce hallucinations, psychoses, and colorful visions. LSD is probably the most powerful hallucinogen of them all. Though mind-expanding qualities have been attributed to it, there is no sound evidence confirming this attribute, as illustrated by the story

Figure 18.8 Illicit dosage forms of lysergic acid diethylamide (LSD). (Courtesy of the U.S. Bureau of Narcotics and Dangerous Drugs, Washington, D.C.)



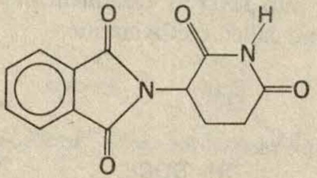
of the guy who took his notebook with him on a trip. While he was airborne, he had a great insight. When he came down he told everyone of his marvelous discovery. He had met ultimate truth, face to face. Finally someone asked what he had learned. He opened his notebook and read, "Green grass is pretty." Now, no one but the most hardened mower of lawns would disagree with the statement, but most people reach that conclusion without chemically "enhancing" their perception. Enhanced creativity is just another drug-induced illusion.

LSD is a potent drug, as indicated by the small amount required for one to experience its fantastic effects. The usual dosage is probably about 10 to 100 μg. No wonder Hofmann had a bad time with 250 μg! To give you an idea of how small 10 μg is, let us compare that amount of LSD to the amount of aspirin in one aspirin tablet. One aspirin tablet contains about 300 000 μg of aspirin. Some common illegal dosage forms of LSD are shown in **figure 18.8.**

Is LSD a dangerous drug? A few facts are known, but most are disputed. In 1967, Maimon Cohen of the State University of New York at Buffalo reported that LSD damages chromosomes, especially those of the leucocytes (white blood cells). The report received wide publicity. Fear of damage to germ cells—and the subsequent birth of deformed babies—caused a decline in the use of LSD. Additional studies produced mixed results. Some seemed to confirm Dr. Cohen's findings. For example, in hamsters, LSD administered to pregnant females caused gross fetal deformities. Other studies, however, seemed to exonerate LSD as a cause of chromosomal damage. The question still has not been resolved.

The great concern over the problem is due, in part, to the thalidomide tragedy of the late 1950s and early 1960s. Thalidomide was a completely legal, amidelike drug used as a tranquilizer.

Figure 18.9 Dr. Frances Kelsey, of the U.S. Food and Drug Administration, discovered that the tranquilizing drug thalidomide caused gross deformities in babies. This discovery in applied research prevented the use of this drug for "morning sickness" and saved many a mother from the tragedy of giving birth to a "thalidomide baby." (Courtesy of the U.S. Food and Drug Administration, Washington, D.C.)

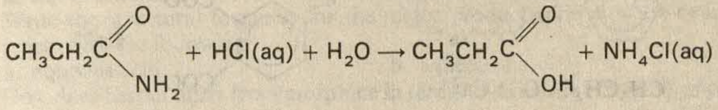


Thalidomide

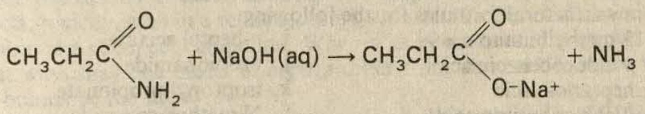
It was considered so safe, based on laboratory studies, that it was widely prescribed for pregnant women and, in Germany, was available without a prescription. It took several years for the human population to provide evidence which laboratory animals did not. The drug had a disastrous effect on developing human embryos. Children born to women who had taken the drug during the first 12 weeks of pregnancy suffered from phocomelia, a condition characterized by shortened or lacking arms or legs and other physical defects. The drug was widely used in Germany and Great Britain, and these two countries bore the brunt of the tragedy. The United States escaped relatively unscathed because an official of the Food and Drug Administration believed there was evidence to doubt the drug's safety and did not, therefore, approve it for use in the United States.

18.13 Chemical Properties of the Amides: Hydrolysis

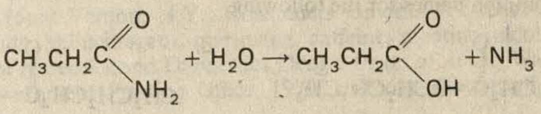
Generally, the amides are neutral compounds, showing neither appreciable acidity nor significant basicity in water. Further, the amides resist hydrolysis in plain water, even upon prolonged heating. In the presence of added acid or base, however, hydrolysis proceeds at a moderate rate. Acidic hydrolysis of a simple amide gives a carboxylic acid and an ammonium salt.



Basic hydrolysis gives a salt of the carboxylic acid and ammonia.



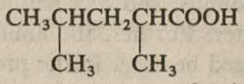
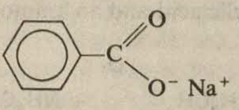
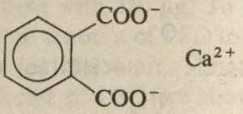
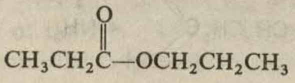
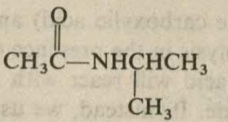
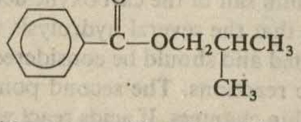
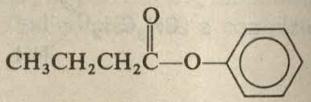
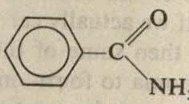
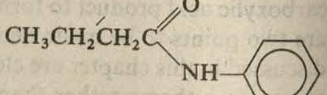
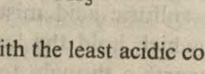
It may be easier to see why the products of the two reactions differ if we consider the hydrolysis products which would form if the reaction could be carried out in the absence of added acid or base.



The products of this reaction are an acid (the carboxylic acid) and a base (ammonia). If we actually carry out the hydrolysis in the presence of hydrochloric acid, then some of the hydrochloric acid will react with the basic product ammonia to form ammonium chloride. If, instead, we use sodium hydroxide to speed the reaction, then some of this base will react with the carboxylic acid product to form the sodium salt of the carboxylic acid. There are two points to be made here. One is that the several hydrolysis reactions discussed in this chapter are closely related and should be considered as variations on a theme rather than separate reactions. The second point is that chemical principles are not confined within chapters. If acids react with bases to form salts in chapter 10, they will also react in chapter 18. If a reaction under consideration happens to produce an acidic product, that product will always exhibit those properties we have previously ascribed to acids.

The hydrolysis of amides is of more than theoretical interest. Digestion of proteins (chapter 29) involves the hydrolysis of amide bonds. Clothes made of nylon, another polyamide, have been known to disintegrate in air polluted with sulfuric acid mist. The acid catalyzes the hydrolysis of the amide bonds which hold the long chains of the nylon molecules together. Perhaps it is worth a thought to consider what that same polluted air does to the proteins of our lungs.

Problems

1. Give the common and the IUPAC name for each of the following.
   a. $HCOOH$
   b. CH_3CH_2COOH
   c. 
   $CH_3\underset{CH_3}{CH}CH_2\underset{CH_3}{CH}COOH$
   d. $CH_3(CH_2)_8COOH$
   e. $HOOCCH_2CH_2CH_2COOH$
2. Give common names for these salts.
   a. 
   b. $(CH_3CH_2COO^-)_2Ca^{2+}$
   c. $CH_3COO^-\ NH_4^+$
   d. $(CH_3CH_2CH_2COO^-)_2Zn^{2+}$
   e. 
3. Draw the simple amide and the methyl ester derived from benzoic acid.
4. Draw structural formulas for the following.
   a. 3-methylbutanoic acid
   b. *p*-chlorobenzoic acid
   c. heptanoic acid
   d. *β*-chlorobutyric acid
   e. *γ*-hydroxyvaleric acid
   f. ethyl butyrate
   g. diethyl oxalate
   h. potassium formate
   i. *n*-heptyl acetate
   j. propionamide
   k. isopropyl propionate
   l. N-methylacetamide
   m. N,N-dimethylbenzamide
   n. phenyl acetate
   o. ethyl benzoate
   p. benzanilide
5. Give common names for the following.
   a. 
   $CH_3CH_2\overset{O}{\overset{\|}{C}}-OCH_2CH_2CH_3$
   b. 
   $CH_3\overset{O}{\overset{\|}{C}}-NH\underset{CH_3}{CH}CH_3$
   c. 
   d. 
   e. 
   f. 
6. Without consulting the tables, arrange these in order of increasing boiling point (place the compound with the lowest boiling point first).
   a. *n*-butyl alcohol b. *n*-pentane c. propionic acid d. methyl acetate
7. From what alcohol might each acid be prepared via oxidation with acidic dichromate (or liver enzymes!)?
   a. CH_3CH_2COOH
   b. $HOOCCOOH$
   c. $HCOOH$
   d. 
   $CH_3\underset{CH_3}{CH}CH_2COOH$
8. Arrange in order of increasing acidity, with the least acidic compound first.
   a. toluene
   b. benzoic acid
   c. benzyl alcohol ($C_6H_5CH_2OH$)

9. Write an equation for the reaction (if any) of each compound with NaOH(aq) and with $NaHCO_3$(aq).
   a. decanoic acid
   b. benzoic acid
   c. benzyl alcohol ($C_6H_5CH_2OH$)

   The three organic starting materials are insoluble in water. What would you observe for each reaction you indicated?
10. Write the structural formulas for the major products formed when ethyl acetate reacts with the following.
    a. water and acid (H^+)
    b. water and base (OH^-)
11. Write the structural formulas for the major product(s) formed when ethyl benzoate reacts with the following.
    a. aqueous acid
    b. aqueous base
12. Write the structural formulas for the major product formed when benzamide reacts with the following.
    a. aqueous acid
    b. aqueous base
13. How does heroin differ from morphine in terms of structure? In terms of physiological properties?
14. Examine the labels of at least five "combination" pain relievers. Make a list of the ingredients in each. Look up the properties (medical use, dosage, side effects, toxicity, etc.) in a reference work such as *The Merck Index*.
15. Aspirin is a chemical compound. What is its structure and chemical name? In what ways may one brand of aspirin differ from another? In what ways must the brands be the same?
16. Do a cost analysis on at least five brands of plain aspirin, calculating the cost per grain. Also calculate the cost per gram (1 g = 15.43 grains).

References and Readings

1. Brecher, Edward M., and the Editors of Consumer Reports, *Licit and Illicit Drugs*, Mount Vernon, N.Y.: Consumers Union, 1972. Discusses stimulants, depressants, hallucinogens, marijuana, caffeine, nicotine, alcohol, and heroin.
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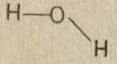
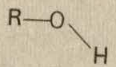
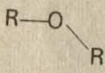
5. Farr, Richard S., "Aspirin: Good News, Bad News," *Saturday Review*, 25 November 1972, pp. 60–63.
6. Hill, John W., *Chemistry for Changing Times*, 2nd ed., Minneapolis: Burgess, 1975. Chapters 16 and 17 cover many drugs affecting the body and the mind.
7. Noller, C. R., *Chemistry of Organic Compounds*, 3rd ed., Philadelphia: W. B. Saunders, 1966. See especially chapters 11 and 28.
8. Windholz, Martha, ed., *The Merck Index*, 9th ed., Rahway, N.J.: Merck, 1976.

chapter 19

Amines and Derivatives

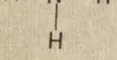

Water


An alcohol

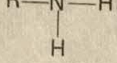

An ether

If carbon compounds are the basis of life, nitrogen compounds are the bases of life (pun intended). Recall from chapter 10 that ammonia is a nitrogen-containing weak base. Amines are alkyl (and aryl) derivatives of ammonia, and they too are weak bases. These organic bases occur in living (and especially in once living but now decaying) organisms.

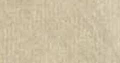
Nitrogen is an essential constituent of many physiologically active compounds. All enzymes—indeed, all proteins—contain nitrogen. Many vitamins and hormones contain nitrogen. Most drugs incorporate nitrogen atoms. And nitrogenous bases are part of the complex structure of the compounds that carry our genetic heritage, the nucleic acids DNA and RNA (bases in acids!). In this chapter we shall discuss the amines generally as well as a number of related nitrogen-containing compounds which exhibit interesting physiological effects. The discussion of proteins and nucleic acids we shall save for later chapters.


$\mathrm{H{-}\underset{\underset{\displaystyle H}{|}}{N}{-}H}$

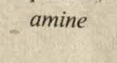
Ammonia


$\mathrm{R{-}\underset{\underset{\displaystyle H}{|}}{N}{-}H}$

A primary amine


$\mathrm{R{-}\underset{\underset{\displaystyle R}{|}}{N}{-}H}$

A secondary amine


$\mathrm{R{-}\underset{\underset{\displaystyle R}{|}}{N}{-}R}$

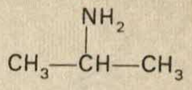
A tertiary amine

We shall also save for subsequent chapters a consideration of the implications of the following facts. Plants can take inorganic nitrogen, usually in the form of nitrate or ammonium salts, and combine it with carbon compounds from photosynthesis to make all the organic nitrogen compounds they require. But animals are not quite so clever. They require some preformed organic nitrogen compounds in their diet, compounds which are essential to their health but which they themselves cannot synthesize.

19.1 Structure and Classification of Amines

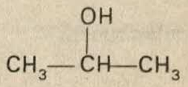
In chapter 16, we saw that the alcohols and ethers can be considered derivatives of water. In a similar manner, the amines are derived from ammonia. Amines are classified according to the number of carbon atoms bonded directly to the nitrogen atom. A primary amine has one alkyl (or aryl) group on the nitrogen, a secondary amine has two, and a tertiary amine has three.

This use of the terms *primary, secondary,* and *tertiary* must be distinguished from our previous use of these terms in connection with the alcohols (section 16.2). For example, consider structures I and II. Compound I is a primary amine because only one of nitrogen's bonds is attached to a carbon atom. But compound II is a *secondary* alcohol. When determining whether an alcohol is primary, secondary, or tertiary, one counts the number of carbons bonded not to the oxygen but to the carbon attached to the oxygen. Another difference can be seen in structures III and IV. Compound III is a secondary amine, but compound IV is an ether (*not* an alcohol, secondary or otherwise). When there is only one carbon group attached to oxygen, the compound is an alcohol. But if there are two, the compound is an ether. In contrast, whether there are one or two (or three) alkyl or aryl groups attached to nitrogen, the compounds are all classed as amines.



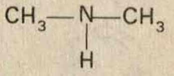
$CH_3-\overset{\overset{\displaystyle NH_2}{|}}{C}H-CH_3$

I



$CH_3-\overset{\overset{\displaystyle OH}{|}}{C}H-CH_3$

II



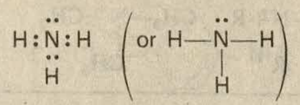
$CH_3-\underset{\underset{\displaystyle H}{|}}{N}-CH_3$

III

CH_3-O-CH_3

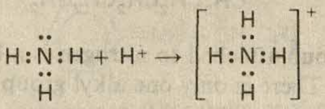
IV

Let's look at the structure of ammonia and the amines a little more closely. In ammonia, three hydrogens are bonded to nitrogen. The nitrogen also has an unshared pair of electrons.



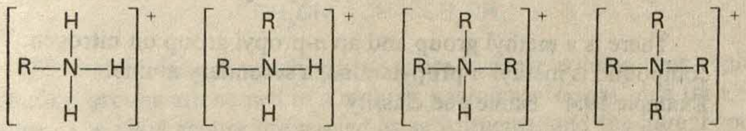
$$H:\underset{\displaystyle H}{\overset{\cdot\cdot}{\underset{\cdot\cdot}{N}}}:H \quad \left(\text{or } H-\underset{\underset{\displaystyle H}{|}}{\overset{\cdot\cdot}{N}}-H\right)$$

Ammonia can undergo a reaction in which it shares its normally nonbonding electrons. It can accept a proton and form the ammonium ion.



$$H:\underset{\displaystyle H}{\overset{\cdot\cdot}{\underset{\cdot\cdot}{N}}}:H + H^+ \longrightarrow \left[H:\underset{\displaystyle H}{\overset{\displaystyle H}{\underset{\cdot\cdot}{\overset{\cdot\cdot}{N}}}}:H\right]^+$$

This, of course, is the reaction of ammonia as a base. An amine also has an unshared pair of electrons, and it too can act as a base. This reaction we shall consider in detail in section 19.5. For the moment, let's concentrate on the fact that, in the ammonium ion, nitrogen is bonded to four different hydrogens. Just as amines are derived from ammonia by replacement of one or several of the hydrogens with alkyl or aryl groups, so too can substituted ammonium ions be derived from the simple ammonium ion. Any or all of the hydrogens on the ammonium ion can be replaced by alkyl (or aryl) groups.



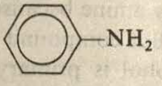
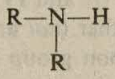
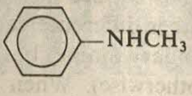
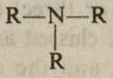
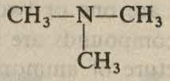
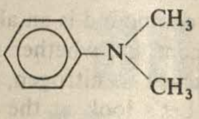
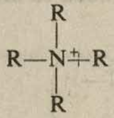
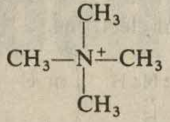
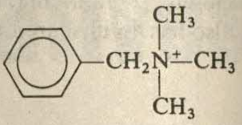
$$\left[R-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{N}}-H\right]^+ \quad \left[R-\overset{\overset{\displaystyle R}{|}}{\underset{\underset{\displaystyle H}{|}}{N}}-H\right]^+ \quad \left[R-\overset{\overset{\displaystyle R}{|}}{\underset{\underset{\displaystyle H}{|}}{N}}-R\right]^+ \quad \left[R-\overset{\overset{\displaystyle R}{|}}{\underset{\underset{\displaystyle R}{|}}{N}}-R\right]^+$$

The ion in which all four hydrogens have been replaced by alkyl groups is termed a *quaternary* ammonium ion. Compounds which incorporate this type of ion are called quaternary ammonium salts (**table 19.1**).

19.2 Naming the Amines

To name simple aliphatic amines, one merely specifies the alkyl groups attached to nitrogen and adds the suffix *-amine*.

Table 19.1
The classification of amines

Class	*Symbol*	*General Formula*	*Examples*	
Primary	1°	$R{-}NH_2$	$CH_3CH_2CH_2NH_2$	
Secondary	2°	 $R{-}\underset{\displaystyle R}{\underset{\vert}{N}}{-}H$	CH_3NHCH_3	
Tertiary	3°	 $R{-}\underset{\displaystyle R}{\underset{\vert}{N}}{-}R$	 $CH_3{-}\underset{\displaystyle CH_3}{\underset{\vert}{N}}{-}CH_3$	
Quaternary (salts)	4°	 $R{-}\overset{\displaystyle R}{\overset{\vert}{\underset{\displaystyle R}{\underset{\vert}{N^{+}}}}}{-}R$	 $CH_3{-}\overset{\displaystyle CH_3}{\overset{\vert}{\underset{\displaystyle CH_3}{\underset{\vert}{N^{+}}}}}{-}CH_3$	

Example 19.1 Name and classify

$$CH_3CH_2CH_2CH_2NH_2$$

The alkyl group attached to nitrogen is *n*-butyl; thus, the name is *n*-butylamine. There is only one alkyl group attached to nitrogen, so the amine is primary.

Example 19.2 Name and classify

$$CH_3CH_2NHCH_2CH_3$$

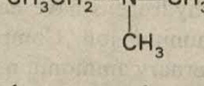
There are two ethyl groups attached to the nitrogen. The compound is diethylamine, a secondary amine.

Example 19.3 Name and classify

$$CH_3NHCH_2CH_2CH_3$$

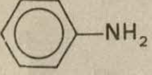
There is a methyl group and an *n*-propyl group on nitrogen. The compound is methyl-*n*-propylamine, a secondary amine.

Example 19.4 Name and classify

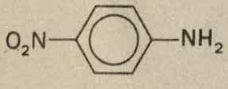


$$CH_3CH_2{-}\underset{\displaystyle CH_3}{\underset{\vert}{N}}{-}CH_3$$

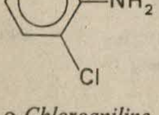
There are two methyl groups and one ethyl group on the nitrogen. The compound is ethyldimethylamine, a tertiary amine.



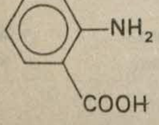
Aniline



p-*Nitroaniline*



o-*Chloroaniline*

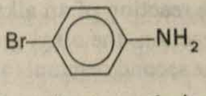


Anthranilic acid

The primary amine in which the nitrogen is attached directly to a benzene ring is called *aniline*. Aryl amines are either named as derivatives of this parent compound or have acquired unique common names (p. 402).

Compounds in which the nitrogen is attached to both a benzene ring and an alkyl group are also named as derivatives of aniline. The alkyl groups are named first, and their position of attachment (i.e., at the nitrogen atom) is indicated by the capital letter *N*.

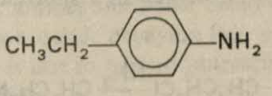
Example 19.5 Name the compound



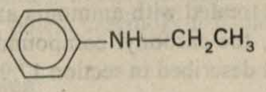
The compound is named as a derivative of aniline. It is *p*-bromoaniline.

Example 19.6 Draw *p*-ethylaniline and N-ethylaniline.

Both compounds are derivatives of aniline. The first compound is a primary amine with an ethyl group located *para* to the *amino* (—NH_2) group.



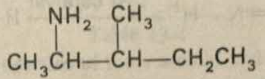
The second compound is a secondary amine with the ethyl group attached at the nitrogen.



For amines which incorporate other functional groups or those in which the alkyl groups cannot be simply named, the amino group is named as a substituent.

Example 19.7 Draw 2-amino-3-methylpentane.

Always start with the parent compound. First draw the five-carbon pentane chaine. Then attach a methyl group at the third carbon atom and an amino group at the second.



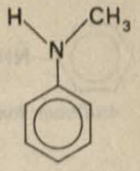
$$CH_3\underset{}{\overset{\overset{NH_2}{|}}{C}}H—\overset{\overset{CH_3}{|}}{C}H—CH_2CH_3$$

Ammonium ions in which one or more hydrogens have been replaced with alkyl groups are named in a manner analogous to that used for simple amines. The alkyl groups are named as substituents, and the parent species is regarded as the ammonium ion.

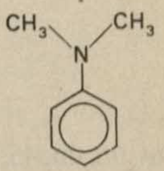
Example 19.8 Name the following ions.

$$CH_3\overset{+}{N}H_3 \quad (CH_3)_2\overset{+}{N}H_2 \quad (CH_3)_3\overset{+}{N}H \quad (CH_3)_4\overset{+}{N}$$

The structures are, in order, methylammonium, dimethylammonium, trimethylammonium, and tetramethylammonium ions.



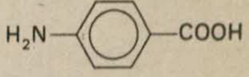
N-Methylaniline



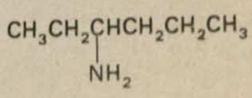
N,N-Dimethylaniline

$H_2N—CH_2CH_2—OH$

2-Aminoethanol (ethanolamine)

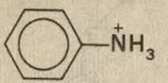


p-*Aminobenzoic acid*



$$CH_3CH_2\underset{\underset{NH_2}{|}}{C}HCH_2CH_2CH_3$$

3-Aminohexane



Anilinium ion

Ions in which one of the ammonium ion's hydrogens has been replaced by a benzene ring are named as anilinium ions instead of ammonium ions. Such ions are prepared (section 19.5) from the corresponding aniline, and the name reflects this fact.

19.3 Making Amines

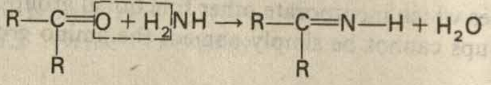
Organic chemists have a variety of methods of making amines. Among the more important is the reaction of an alkyl halide with ammonia or with another amine. In this reaction, the alkyl group of the halide is transferred to the nitrogen atom of the second reactant (ammonia in the equation below).

$$RCl + 2\,NH_3 \rightarrow RNH_2 + NH_4Cl$$

A by-product of the initial reaction is hydrogen chloride, but this product immediately reacts with excess ammonia to form the ammonium chloride by-product shown in the equation. As is frequently done in organic chemistry, the equation may be written in a shorthand form which ignores this inorganic by-product.

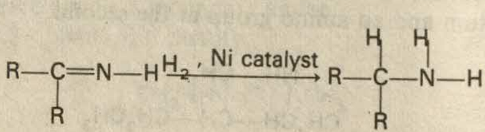
$$CH_3CH_2Cl \xrightarrow{NH_3} CH_3CH_2NH_2$$

A second general method of preparing amines, called *reductive amination,* is a combination of two reactions we have encountered previously. A carbonyl compound is treated with ammonia and hydrogen in the presence of a catalyst. Initially, the carbonyl compound reacts with ammonia in a reaction similar to that described in section 17.9.



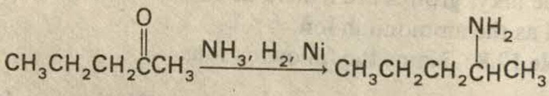
$$R{-}\underset{R}{C}{=}\boxed{O + H_2}NH \rightarrow R{-}\underset{R}{C}{=}N{-}H + H_2O$$

The double bond of the intermediate product is then reduced by the hydrogen-catalyst combination used previously with alkenes (section 14.11).



$$R{-}\underset{R}{C}{=}N{-}H \xrightarrow{H_2,\ \text{Ni catalyst}} R{-}\overset{H}{\underset{R}{C}}{-}\overset{H}{N}{-}H$$

Overall, the reaction involves the conversion of an aldehyde or ketone group to an amino group.



$$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow{NH_3,\ H_2,\ Ni} CH_3CH_2CH_2\overset{NH_2}{\overset{|}{C}}HCH_3$$

The reaction is of great interest to chemists because it is versatile and frequently gives high yields of desired products. But we mention it particularly because living systems use a similar reaction sequence to convert carbonyl groups to amine groups. The reagents these systems use differ somewhat from those we've shown, and the catalysts are enzymes rather than metals, but the sequence of transformations is essentially the same as in reductive amination.

19.4 Physical Properties of Amines

Primary and secondary amines have hydrogen on nitrogen; thus, they are capable of intermolecular hydrogen bonding. These forces are not as strong as those between alcohol molecules (which have hydrogen on oxygen, a more electronegative element than nitrogen). Amines boil at higher temperatures than alkanes but at lower temperatures than alcohols of comparable molecular weight. Tertiary amines have no hydrogen on nitrogen and cannot form intermolecular hydrogen bonds. They have boiling points comparable to those of the ethers.

All three classes of amines can hydrogen bond to water. Amines of low molecular weight are quite soluble in water, the borderline of water solubility coming at five or six carbon atoms.

Amines have interesting (!) odors. The simple ones smell very much like ammonia. Higher aliphatic amines smell like decaying fish. Or perhaps we should put it the other way around: decaying fish give off odorous amines. The stench of rotting flesh is due in part to putrescine and cadaverine, two compounds which are diamines.

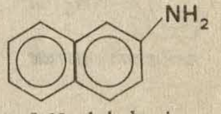
Aromatic amines generally are quite toxic. They are readily absorbed through the skin, and you must take care to prevent serious accidents when working with these compounds. Several aromatic amines, including especially β-naphthylamine, are potent carcinogens (cancer-inducing chemicals).

$H_2NCH_2CH_2CH_2CH_2NH_2$

1,4-Diaminobutane (putrescine)

$H_2NCH_2CH_2CH_2CH_2CH_2NH$

1,5-Diaminopentane (cadaverine)



β-Naphthylamine

19.5 The Amines as Bases

As we noted in section 19.1, ammonia is basic; it can accept a proton from water to form ammonium ions and hydroxide ions.

$$:NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^-$$

Ammonia is a weak base; this equilibrium strongly favors the un-ionized forms. Similarly, the amines have an unshared electron pair on nitrogen and can accept protons.

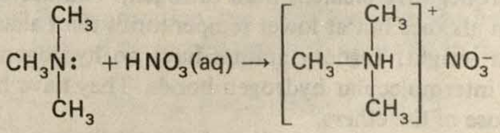
Table 19.2
Physical properties of some amines and comparable oxygen-containing compounds

Compound	*Class*	*Molecular Weight*	*Boiling Point (in degrees Celsius)*
n-Butylamine	1°	73	78
Diethylamine	2°	73	55
n-Butyl alcohol	—	74	118
n-Propylamine	1°	59	49
Trimethylamine	3°	59	3
Ethyl methyl ether	—	60	6

$$CH_3\ddot{N}H_2 + H_2O \rightleftharpoons [CH_3NH_3]^+ + OH^-$$

Simple aliphatic amines are somewhat more basic than ammonia, although still much less basic than compounds such as sodium hydroxide. Aromatic amines, such as aniline, are much weaker bases than even ammonia.

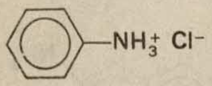
Amines react readily with strong acids, such as the mineral acids, to form salts.



$$(CH_3)_3N: + HNO_3(aq) \longrightarrow [(CH_3)_3NH]^+ \; NO_3^-$$

Trimethylamine *Trimethylammonium nitrate*

Amine salts are named like other salts: the name of the cation is given first, followed by that of the anion. Remember that the ions formed from aliphatic amines are named as substituted ammonium ions (example 19.8).

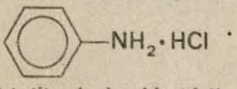


Anilinium chloride

Example 19.9 Name the salt

$$[CH_3NH_2CH_2CH_3]^+ \; CH_3COO^-$$

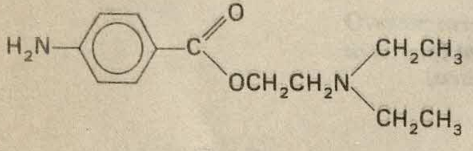
The cation has a methyl and an ethyl group attached to nitrogen and is, therefore, the ethylmethylammonium ion. The anion is the acetate ion. The salt is therefore ethylmethylammonium acetate.



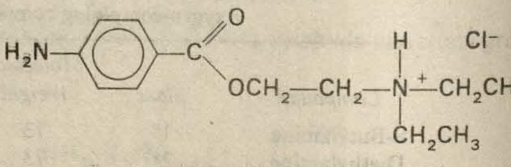
"Aniline hydrochloride"

Salts of aniline are named as anilinium compounds. An older system, still in use for naming drugs, calls the salt of aniline and hydrochloric acid "aniline hydrochloride." By this older system, the formula of the compound is frequently drawn to correspond to the name. Keep in mind that these compounds are really ionic—they are salts—even though the name and formula seem to indicate a loose association of molecules. The properties of the compounds (solubility, for example) are those characteristic of salts.

Physiologically active amines are often converted to salts and thereby rendered water soluble. For instance, procaine is soluble only to the extent of 0.5 g in 100 g of water. The hydrochloride is soluble to the remarkable degree of 100 g in 100 g of water.



Procaine

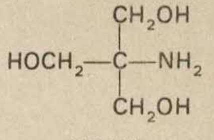


*Procaine hydrochloride (*Novocaine*)*

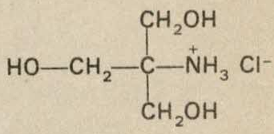
Procaine hydrochloride, perhaps better known by the trade name *Novocaine*, is widely used as a local anesthetic.

You know that a weak acid and its salt (e.g., acetic acid and sodium acetate) can be used in the preparation of buffer solutions (section 11.5).

Similarly, amines and their salts can also be used in the preparation of buffers. Whereas the acid/acid salt combination yields a solution which is buffered at acidic pH values, the amine/amine salt buffer will stabilize the pH in a basic range. An important example is tris(hydroxymethyl)aminomethane, often called simply "tris." This compound and its salt, tris hydrochloride, buffer in the range of 7 to 9 pH units. These compounds find wide use in cosmetic and textile chemistry, in cleaning compounds, and in biochemical research. "Tris" is also used in the treatment of metabolic acidosis.



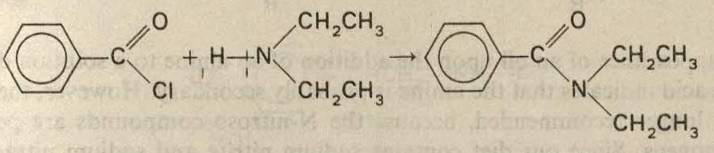
"Tris"



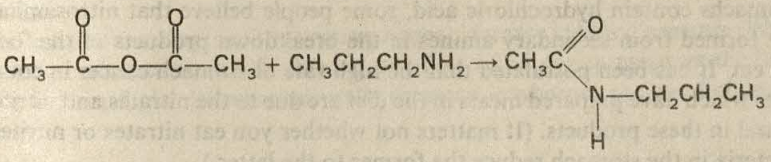
Tris hydrochloride

19.6 Other Chemical Properties of the Amines

In the preceding section we saw that water-soluble amines give basic solutions and that amines generally react with mineral acids to form salts. In chapter 18, the preparation of substituted amides from amines was mentioned. Primary or secondary amines can react with acid chlorides or acid anhydrides to form amides with substituents on the nitrogen atom.

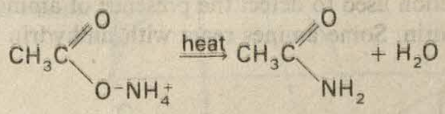


Benzoyl chloride *Diethylamine* *N,N-Diethylbenzamide*



Acetic anhydride n-*Propylamine* *N*-n-*Propylacetamide*

Amides are also made by heating of ammonium salts of carboxylic acids.



Ammonium acetate *Acetamide*

These and similar reactions are of considerable importance in the synthesis of proteins (chapter 24), plastics (chapter 21), and medicinals.

We shall consider two additional reactions of amines—reactions of considerable importance to those studying biological processes. First, amines react with nitrous acid. The nature of the products depends on the class of the amine involved. Primary amines give a quantitative yield of nitrogen gas.

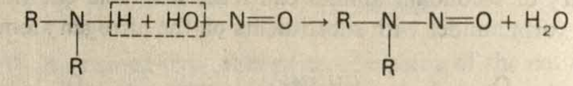
$$R{-}NH_2 + HNO_2 \longrightarrow N_2(g) + \text{other products}$$

Nitrous acid is unstable, so it is usually made *in situ* (right in the reaction vessel) by addition of hydrochloric acid to sodium nitrite.

$$NaNO_2(aq) + HCl(aq) \longrightarrow HNO_2(aq) + NaCl(aq)$$

When a primary amine is added to this solution, bubbles of nitrogen gas can be seen escaping. These bubbles are an indication that the amine is a primary one, because secondary and tertiary amines do not release nitrogen gas. Therefore, this reaction serves as a qualitative test for primary amines. If the amount of the original amine is carefully measured and the nitrogen is collected and its volume measured and corrected to conditions of standard temperature and pressure, the reaction can be used for the quantitative determination of primary amino groups. One molecule of nitrogen (N_2) is liberated for each free amino group. The procedure is referred to as the *Van Slyke method* and is used especially with amino acids and proteins.

Secondary amines react with nitrous acid to form oily N-nitroso compounds.

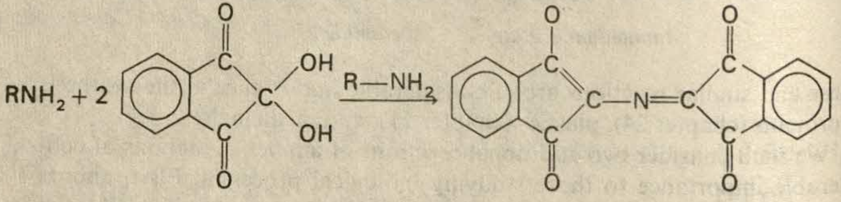


$$R{-}\underset{\displaystyle R}{\underset{|}{N}}{-}\boxed{H + HO}{-}N{=}O \longrightarrow R{-}\underset{\displaystyle R}{\underset{|}{N}}{-}N{=}O + H_2O$$

The appearance of an oil upon the addition of an amine to a solution of nitrous acid indicates that the amine is probably secondary. However, the test is no longer recommended, because the N-nitroso compounds are potent carcinogens. Since our diet contains sodium nitrite and sodium nitrate as food additives (read the label on a package of hot dogs sometime) and our stomachs contain hydrochloric acid, some people believe that nitrosamines are formed from secondary amines in the breakdown products of the food we eat. It has been postulated that the high rate of stomach cancer in countries which have prepared meats in the diet are due to the nitrates and nitrites found in these products. (It matters not whether you eat nitrates or nitrites; bacteria in the stomach reduce the former to the latter.)

Tertiary amines also react with nitrous acid. Generally, the only product is a salt. Sometimes, though, the tertiary amine is cleaved to a secondary one which then can form a nitroso derivative.

A second reaction used to detect the presence of amines is that with the compound ninhydrin. Some amines react with ninhydrin to form a purple to blue anion.

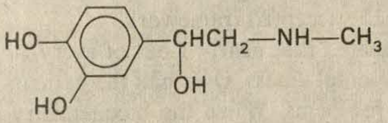


The ninhydrin test is especially suited to the detection of amino acids. Mixtures of amino acids, such as those which result from the hydrolysis of proteins, can be separated by a process called paper chromatography. At the conclusion of such a separation, the individual amino acids are scattered at different locations on the paper chromatogram. The amino acid cannot be seen, however, until the chromatogram is sprayed with ninhydrin and the colored ion becomes visible. Then the position of the constituents of the original mixture can be compared to those of known amino acids, and an identification can be made on this basis.

19.7 Brain Amines: The Ups and Downs of Life

We all have our ups and downs in life. Recent attempts have been made to quantify these as biological rhythms (references 7 and 8). Women seem to go through emotional states closely related to the menstrual cycle, with "highs" occurring in the early part of the cycle and depression deepening toward the onset of menses. These subjective emotional states may well be related to the flow of the female sex hormones (chapter 27). Perhaps surprisingly, men also seem to go through monthly cycles. These may be related to the secretion of certain adrenal steroids.

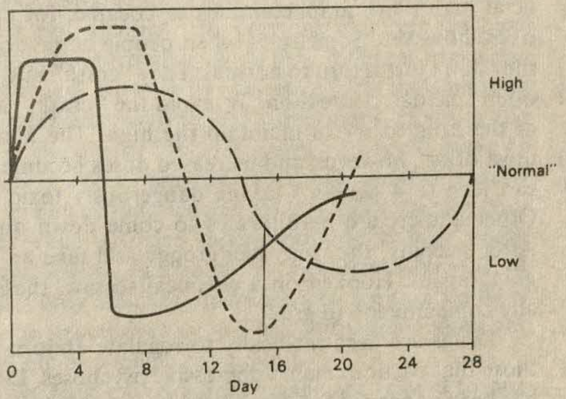
Certain other hormones may also be involved. One well-known compound, epinephrine, commonly called adrenalin, is secreted by the adrenal glands.



Epinephrine (adrenalin)

A tiny amount of epinephrine causes a great increase in blood pressure. When one is under stress or is frightened, the flow of adrenalin prepares the body for fight or flight. Because culturally imposed inhibitions prevent fighting or

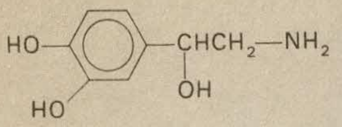
Figure 19.1 Effects of drugs on the mental state of an individual. The diagram is illustrative only and should not be interpreted literally.



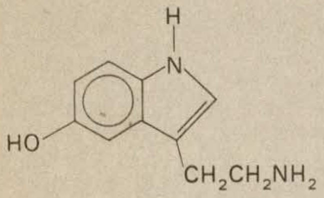
— — = "normal" ups and downs, perhaps controlled by serotonin and norepinephrine

- - - = manic-depressive psychoses, in which ups and downs last for varying periods of time

—— = a drug-induced high, maintained for a few days before a "crash." A person who stays off drugs will slowly return to a "normal" cycle



Norepinephrine



Serotonin

fleeing in most modern situations, the **adrenalin-induced supercharge** is not used. This sort of frustration has been implicated in some forms of mental illness.

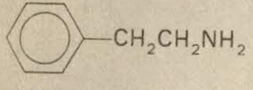
One widely held theory of a biochemical basis for mental illness involves a relative of epinephrine, norepinephrine, and another hormone, serotonin. Whereas norepinephrine, like epinephrine, is a powerful stimulant, serotonin is a depressant. A normal mental condition involves a delicate balance of the two compounds in the brain. When something happens in the biochemistry of the body to cause an excess of serotonin in the brain, a person is depressed. The greater the excess, the greater the depression. If, on the other hand, norepinephrine is formed in excess, the person is in an elated, perhaps hyperactive state. In large excess, norepinephrine could cause a *manic* state.

There is some experimental basis for the molecular theory of mental illness (for example, the mind-bending drug LSD forms a chemical complex with serotonin), but it is a *theory* and must be regarded as tentative. It serves as a temporary framework on which one can place a few known facts and within which one can propose and perform new experiments. Quite often, however, really big breakthroughs come when someone dares to think or experiment outside the accepted framework.

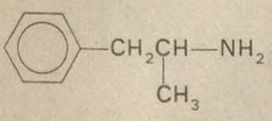
Figure 19.2 A *Benzedrine* inhaler, 1932. Abuse led to the banning of the inhaler. (Courtesy of the U.S. Bureau of Narcotics and Dangerous Drugs, Washington, D.C.)

It has been estimated that nearly 1 out of every 10 people in the United States suffers from mental illness. Over half the patients in hospitals are there because of mental problems. When the biochemistry of the brain is more fully understood, mental illness may be cured (or at least alleviated) by administration of drugs. In the remainder of this chapter we shall see just how far we have already come in learning to control our moods with drugs. As is true for so many things, the potential for good which such compounds represent is matched by their potential for abuse.

One can readily see how the use of drugs would affect mental cycles. Chemicals can induce artificial highs or lows (**figure 19.1**). Achieving an artificial high (with amphetamines or cocaine, for example) is not without its risks, however. Sometimes when people come down from a chemical high, they don't just return to normal. They "crash" into an abnormal low—a deep, often suicidal, depression. To avoid the "crash," a user often will take more of the drug to try to maintain the high. The body develops a tolerance to most drugs, however, and increased doses become necessary. Such a buildup can lead to a person's taking dangerously toxic levels—and to psychoses. Other addicts use barbiturates to come down quickly and to get to sleep. After sleeping, they may feel groggy and take an "upper" to help them get going again. Hooked on a chemical seesaw, these unfortunate people usually come quickly to grief.

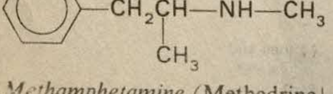


β-Phenylethylamine



*Amphetamine (*Benzedrine*)*

Drugs are used medically to regulate abnormal highs and lows such as those that occur in manic-depressive psychoses. **Lithium carbonate** (Li_2CO_3) has been approved for use in leveling out the dangerous manic stage. **Psychic energizers** such as imipramine (section 19.12) can be used to combat deep depression.



*Methamphetamine (*Methedrine*)*

Among the more widely known stimulants are a variety of synthetic amines, all related to β-phenylethylamine. Note the similarity in structure of these synthetic amines to the natural stimulants, epinephrine and norepinephrine (pp. 409, 410). All are derived from the basic β-phenylethylamine structure. Perhaps the amphetamines act as stimulants by mimicking the natural brain amines.

Amphetamine and methamphetamine have been widely abused. Amphetamine has been extensively used for weight reduction. It has also been employed for treating mild depression and narcolepsy, a rare form of sleeping sickness. Amphetamine induces excitability, restlessness, tremors, insomnia, dilated pupils, increased pulse rate and blood pressure, hallucinations, and psychoses. It is no longer recommended for weight reduction. It was found that, generally, any weight loss was only temporary. The greatest problem, however, was the diversion of vast quantities of amphetamines into the illegal drug market. Amphetamines are inexpensive. Armed forces personnel, truck drivers, and college students have been among the heavy users. Some of the slang names originated among truck drivers, who called the amphetamines "coast to coasts" and "copilots." They are also called "bennies" and "pep pills," and by a variety of names descriptive of the shape or color of the pill, such as "peaches," "roses," or "hearts."

Methamphetamine has a more pronounced psychological effect. Generally, it is the "speed" that abusers inject into their veins. Such injections, at least initially, are said to give the individual a euphoric "rush." Shooting methamphetamine is quite dangerous, though, because it is rather toxic.

Dextroamphetamine (*Dexedrine*) is another stimulant drug which has been widely abused. It is structurally related to amphetamine in a quite subtle way. Actually, amphetamine is not a single compound but a mixture of two isomers. These isomers have the same atoms and same groups of atoms, but they are oriented differently in space. One isomer is the mirror image of the other, so that, if the dotted line in **figure 19.4** were the surface of a mirror, then the reflection in the mirror of the right-hand compound would look like the left-hand compound. These isomers are not superimposable; therefore, they are not identical. In previous chapters we have emphasized the fact that structural formulas which look different may actually represent the same compound. Now we have a set of formulas that look pretty much alike but that represent two different compounds. If you could build a model of each one of the mirror image isomers, you could prove to yourself that they cannot be made to coincide with one another exactly (cannot be superimposed). In lieu of that, we can at least show you for contrast a set of mirror images which are also superimposable, that is, which represent a single compound. **Figure 19.5** shows β-phenylethylamine itself and its mirror image. It takes only a cursory inspection to see that we have simply drawn exactly the same structure twice. β-Phenylethylamine does not exist as a mixture of isomers but as a single compound.

The two isomers which we have called amphetamine are related to one another in much the same way that your right hand is related to your left. You can't fit a right-hand glove on your left hand or vice versa. Similarly, the mirror image amphetamine isomers fit enzymes differently and thus have different physiological effects. The dextro ("right-handed") isomer is a stronger stimulant than the levo ("left-handed"). *Dexedrine* is the trade name for the pure dextro isomer. *Benzedrine* is the trade name for a mixture of

Figure 19.3 Amphetamine tablets. (Courtesy of the U.S. Bureau of Narcotics and Dangerous Drugs, Washington, D.C.)

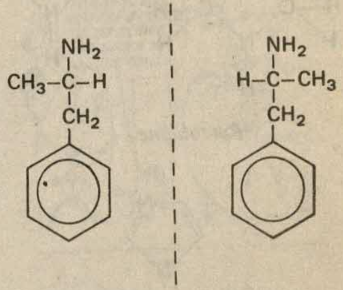


Figure 19.4 Mirror image isomers of amphetamine.

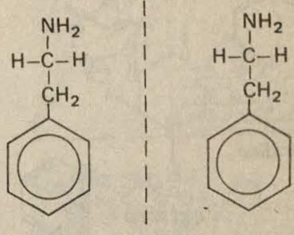
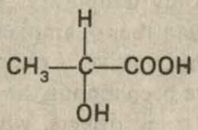


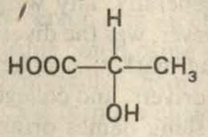
Figure 19.5 Mirror images of β-phenylethylamine.

the two isomers in equal amounts. *Dexedrine* is two to four times as active as *Benzedrine.*

Mirror image isomerism is quite common in organic chemicals of biological importance. Usually only one of the two isomers occurs in nature; thus, for many purposes, it is not necessary to emphasize the isomerism. Generally, molecules which have four different groups attached to a single carbon atom can exist as mirror image isomers. Lactic acid is a familiar compound which fits this description.



$$CH_3-\overset{H}{\underset{OH}{C}}-COOH$$

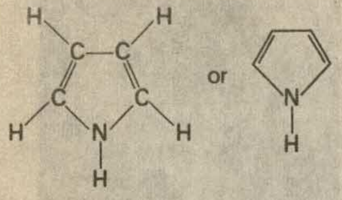


$$HOOC-\overset{H}{\underset{OH}{C}}-CH_3$$

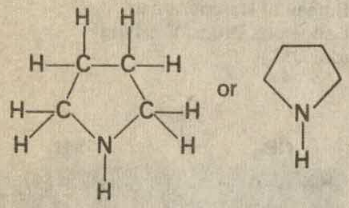
The dextro isomer occurs in blood and muscle tissue, where it is formed by the oxidation of glucose. Levo lactic acid occurs in sour milk. The type of isomerism represented by lactic acid will be considered again in chapter 22.

19.8 Heterocyclic Amines: Nitrogen "Sets" in Carbon Rings

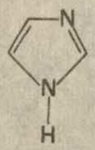
In chapter 14 we encountered a variety of cyclic hydrocarbons. All the atoms in the rings of these compounds were carbon atoms. There are other cyclic compounds in which the molecules have nitrogen, oxygen, sulfur, or other elements in the rings. These are called *heterocyclic* compounds; those rings with only carbon atoms are called *carbocyclic* compounds. In this section we will consider a variety of heterocyclic amines, compounds of considerable importance.



Pyrrole

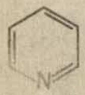


Pyrrolidine

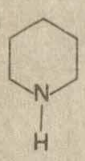


Imidazole

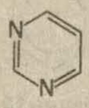
The compounds pyrrole and pyrrolidine each have four carbon atoms and one nitrogen atom in a ring. Pyrrole is an aromatic compound, having properties similar to those of benzene. Pyrrolidine, with four more hydrogen atoms than pyrrole, behaves like an aliphatic amine. Imidazole also has a five-membered ring, but it contains two nitrogen atoms and only three carbon atoms. Like pyrrole, imidazole has aromatic properties.



Pyridine

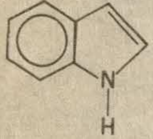


Piperidine

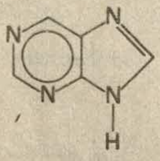


Pyrimidine

Pyridine and piperidine each have five carbon atoms and one nitrogen atom. Pyridine is aromatic; piperidine is aliphatic. Another six-membered heterocycle is pyrimidine, which has two nitrogen atoms and four carbon atoms. Pyrimidine is another aromatic compound.



Indole



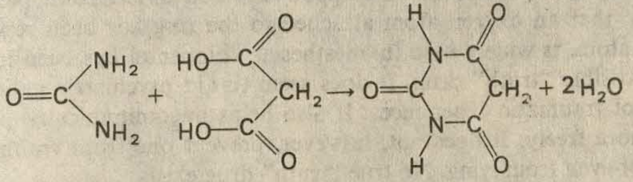
Purine

Other heterocyclic compounds have two rings which share a common side (a situation we encountered with naphthalene among the carbocyclic compounds). Indole has a benzene ring fused with a pyrrole ring. Purine has a pyrimidine ring sharing a side with an imidazole structure. Bases related to purine and pyrimidine make up a part of the structure of the nucleic acids, compounds which comprise the genetic material of cells and which direct protein synthesis. Nucleic acids will be discussed in chapter 25. At that time we shall encounter one of the truly outstanding examples of the critical importance of the shape of molecules and of the importance of molecular structure in general.

19.9 Barbiturates: Sedation, Sleep, and Suicide

As a family of related compounds, the barbiturates display a wide variety of properties. They produce mild sedation, deep sleep, and even death.

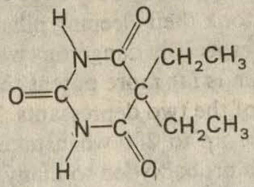
Barbituric acid was first synthesized in 1864 by Adolph von Baeyer, a young student of August Kekulé (chapter 14). Baeyer made it from urea and malonic acid. Urea occurs in urine; malonic acid is derived from apples.



Urea *Malonic acid* *Barbituric acid*

The story goes that the compound was discovered on the day of Saint Barbara. The name is supposedly derived from the words *Barbara* and *urea*.

The medicinal value of the barbiturates was discovered in 1903 by Joseph von Mering. A derivative, called barbital, was found to be useful in putting dogs to sleep.

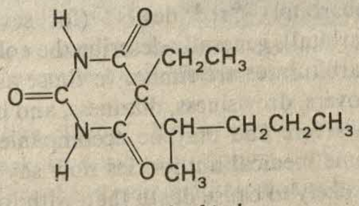


Barbital

The barbiturates are actually cyclic amides (not amines), but notice that the barbiturate ring resembles that of pyrimidine. Recent evidence indicates that the barbiturates may act by substituting for the pyrimidine bases in nucleic acids, thus interfering with protein synthesis.

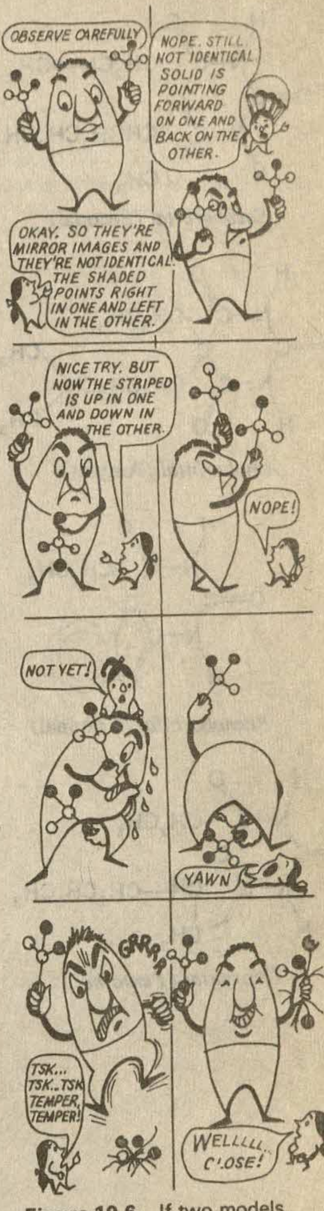
Several thousand barbiturates have been synthesized through the years, but only a few have found widespread use in medicine.

Pentobarbital (*Nembutal*) is employed as a short-acting hypnotic drug.



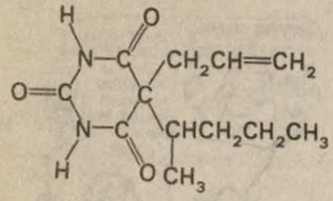
Pentobarbital

Before the discovery of modern tranquilizers, pentobarbital was widely used as a calmative against anxiety and other disorders of psychic origin.

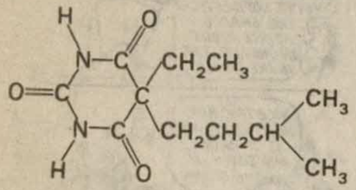


OBSERVE CAREFULLY
NOPE. STILL NOT IDENTICAL. SOLID IS POINTING FORWARD ON ONE AND BACK ON THE OTHER.
OKAY. SO THEY'RE MIRROR IMAGES AND THEY'RE NOT IDENTICAL. THE SHADED POINTS RIGHT IN ONE AND LEFT IN THE OTHER.
NICE TRY. BUT NOW THE STRIPED IS UP IN ONE AND DOWN IN THE OTHER.
NOPE!
NOT YET!
YAWN
GRRRR
TSK... TSK...TSK TEMPER, TEMPER!
WELLLLL... CLOSE!

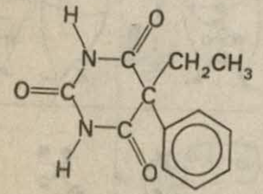
Figure 19.6 If two models which are mirror images of one another cannot be made to coincide exactly with one another, they represent actual isomers.



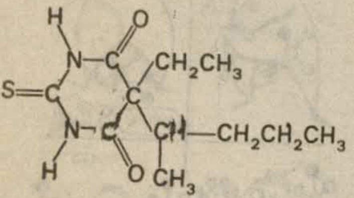
Secobarbital (Seconal)



Amobarbital (Amytal)



Phenobarbital (Luminal)



Thiopental (*Pentothal*)

Another short-acting barbiturate is secobarbital (*Seconal*). It is used as a hypnotic and sedative. Phenobarbital (*Luminal*) is a long-acting drug. It, too, is a hypnotic and can be used as a sedative. Phenobarbital is widely employed as an anticonvulsant for epileptics and people suffering from brain damage. The action of amobarbital (*Amytal*) is intermediate in duration relative to secobarbital and phenobarbital.

Thiopental (*Pentothal*), a compound which differs from pentobarbital only in that an oxygen atom attached to the ring has been replaced by a sulfur atom, is widely used in anesthesia. Thiopental has been investigated as a possible "truth" drug. It does seem to aid psychiatric patients in the recall of traumatic experiences. It also helps uncommunicative individuals talk more freely. It does not, however, prevent one from withholding the truth or even from lying. No true "truth" drug exists.

The barbiturates were once used in small dosages as sedatives. The dosage for sedation was generally a few milligrams. In larger dosages (of about 100 mg), the barbiturates induce sleep. They are the sleeping pills so widely used—and abused—by middle-class, often middle-aged, people. The lethal dose is in the vicinity of 1500 mg (1.5 g). Barbiturates are the drug of choice for most suicides. News reports list the cause of death as "an overdose of sleeping pills." There is also a potential for accidental overdose. After taking a couple of tablets, individuals may be groggy but not yet asleep. Unable to remember whether they took their sleeping pills or not, they take more.

The barbiturates are especially dangerous when ingested along with ethyl alcohol. This combination is far more potent than one would judge by simply summing the effects of the two depressants. The effect of the barbiturate is enhanced by factors of up to 200 when taken with alcoholic beverages. This synergistic effect has probably led to many deaths. We will never know how often alcohol is involved in deaths reported as due to "an overdose of sleeping pills." **Synergistic** effects are not limited to alcohol-barbiturate combinations. One should never take two drugs at the same time without competent medical supervision.

The barbiturates are strongly addictive. Habitual use leads to the development of a tolerance to the drug. One requires ever-larger doses to get the same degree of intoxication. Barbiturates are legally available by prescription only, but they are a part of the illegal drug scene also. Generally, they are known as "downers" because of their depressant, sleep-inducing effects. They are also called "goof balls." Other names, such as "yellow jackets" (for pentobarbital), "red devils" (for secobarbital), and "blue heavens" (for amobarbital), generally describe the color of the capsules.

Side effects of barbiturates are similar to those associated with alcohol. Abuse leads to hangovers, drowsiness, dizziness, and headaches. Withdrawal symptoms are often severe and may be accompanied by convulsions and delirium. In fact, some medical authorities now say that withdrawal from barbiturates is more likely to cause death than withdrawal from heroin.

19.10 Some Alkaloids of Interest: From Caffeine to Cocaine

Many amines, particularly heterocyclic ones, occur naturally in plants. Like most amines, these compounds are basic. They are called *alkaloids* a

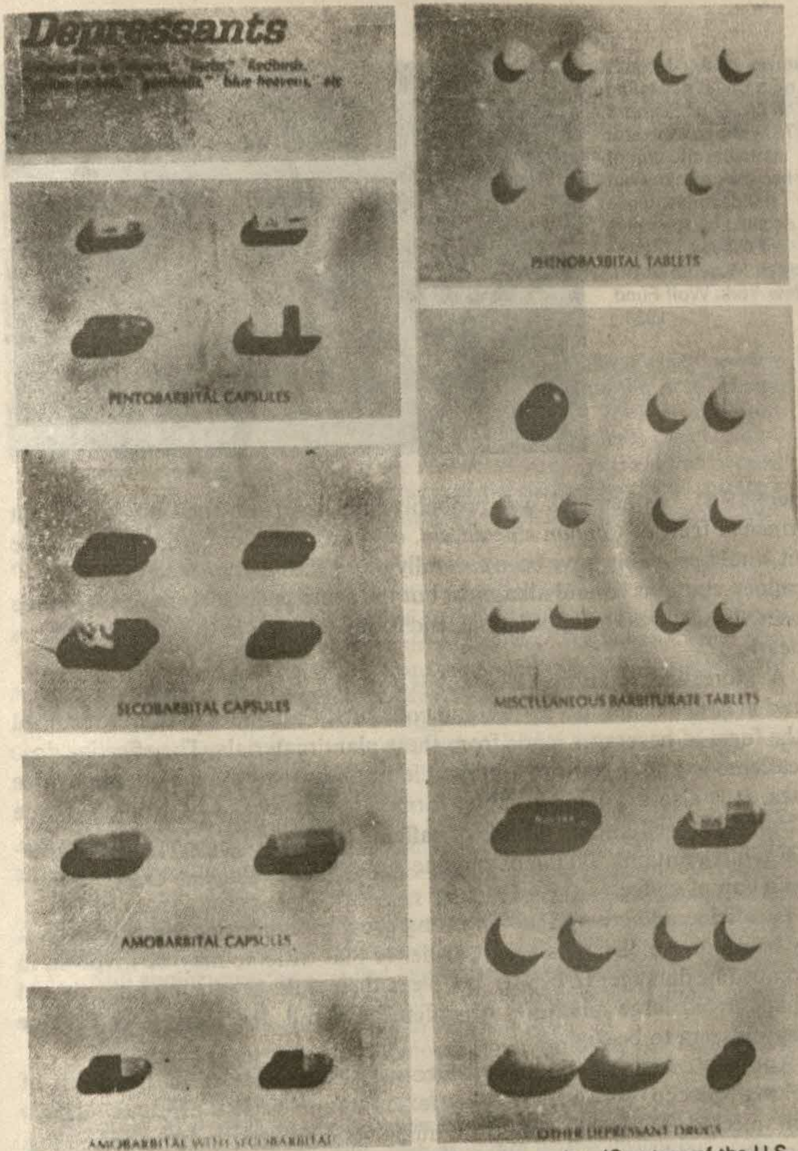


Figure 19.7 Miscellaneous barbiturate tablets and capsules. (Courtesy of the U.S. Bureau of Narcotics and Dangerous Drugs, Washington, D.C.)

name which means "like alkalis." Knowledge of many of these, at least in crude form, dates back to antiquity. Opium, which contains about 10% morphine (chapter 18) as the principal alkaloid, has been used for thousands of years, although morphine was not isolated until 1805.

When the Greek philosopher Socrates was accused of corrupting the youth of Athens in 399 B.C., he was given the choice of exile or death. He chose the latter and implemented his decision by drinking a cup of hemlock

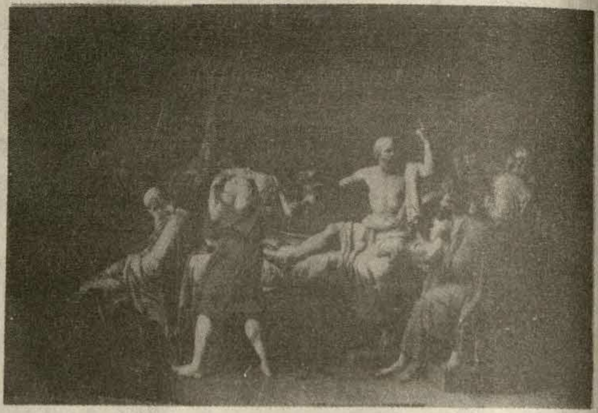
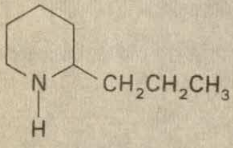


Figure 19.8 Jacques Louis David's painting *The Death of Socrates* (1787) shows Socrates drinking the cup of hemlock to carry out the death sentence decreed by the rulers of Athens. (Metropolitan Museum of Art, New York. Wolf Fund, 1931.)

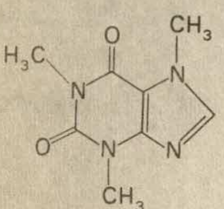
(**figure 19.8**). His hemlock was probably prepared from the fully grown but unripened fruit of *Conium maculatum*, or poison hemlock (**figure 19.9**). The fruit would probably have been carefully dried and then brewed into a "tea." Hemlock contains several alkaloids, but the principal one is coniine. Coniine causes nausea, weakness, paralysis, and ultimately—as in the case of Socrates —death.



Coniine

A more widely known alkaloid is caffeine, a mild stimulant which is found in coffee beans, tea leaves, and cola nuts. Caffeine is usually consumed in the form of beverages made from these plant materials. The effective dose of caffeine is about 200 mg, obtainable in about two cups of strong coffee or tea. It is also available in tablet form as a stay-awake or keep-alert type of drug. Two well-known brands of caffeine tablets are *No-Doz* and *Vivarin*. Each tablet contains 100 mg of caffeine—about the same amount of caffeine as in a cup of coffee.

Is caffeine addictive? The "morning grouch" syndrome indicates that it may be mildly so. There is recent evidence that caffeine may be involved in chromosome damage. To be safe, people in their child-producing years should perhaps avoid large quantities of caffeine. Overall, the hazards of caffeine ingestion seem to be slight.

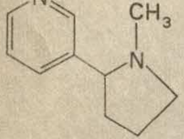


Caffeine

Another common alkaloid is nicotine, usually taken in the form of smoking tobacco. Nicotine is highly toxic to animals. It is especially deadly when injected. The lethal dose for a human is estimated to be about 50 mg. Nicotine is used in agriculture as a contact insecticide.

Nicotine seems to have a rather transient effect as a stimulant. This initial response is followed by depression.

Is nicotine addictive? Casual observation of a person who is trying to quit smoking seems to indicate that it is. There is also evidence of the development of tolerance. It is difficult, however, to separate all the social factors involved in smoking from the physiological effects.



Nicotine

Cocaine is another well-known alkaloid. This drug was first isolated in 1860 from the leaves of the coca plant (**figure 19.10**). Its structure was determined by Richard Willstätter in 1898. Cocaine is a powerful stimulant.

Many of the Indians living on and around the eastern slopes of the Andes Mountains chew the leaves of the coca plant—mixed with lime and ashes—for their stimulant effect. Cocaine usually arrives in the United States as glistening white crystals; hence the slang name "snow." Some cocaine is legally imported for legitimate human and veterinary medical purposes. A far greater quantity is smuggled in for the illegal drug market.

Cocaine stimulates mental activity and quickens the reflexes. It increases stamina and reduces fatigue. Moreover, it gives the user a feeling of confi-

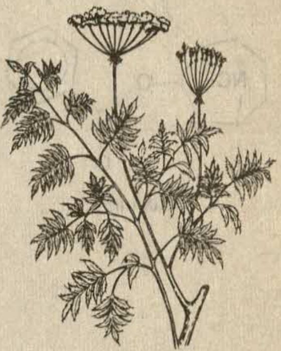


Figure 19.9 *Conium maculatum* (poison hemlock).

A *general anesthetic* acts on the brain to produce unconsciousness as well as insensitivity to pain. Diethyl ether (chapter 16) was the first general anesthetic. It was introduced into surgical practice in 1846 by a Boston dentist, William Morton. Inhalation of ether vapor produces unconsciousness by depressing the activity of the central nervous system. Ether is relatively safe. There is a fairly wide gap between the effective level for anesthesia and the lethal dose. The disadvantages are high flammability and a side effect of nausea.

Chloroform (chapter 15) was introduced as a general anesthetic in 1847. It was widely used for years. It is nonflammable and produces effective anesthesia, but has a number of serious drawbacks. For one, it has a narrow safety margin: the effective dose is close to the lethal dose. It also causes liver damage. It must be protected from oxygen during storage to prevent the formation of deadly phosgene gas.

Divinyl ether (chapter 16) was suggested as an anesthetic in 1930. It is about seven times as effective as ethyl ether. It also acts more rapidly but has the disadvantage of reaching too deep an anesthesia too rapidly. Like its relative, diethyl ether, divinyl ether is extremely flammable.

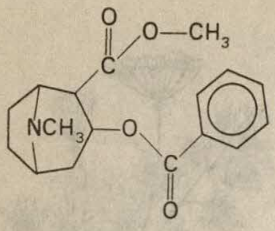
The most potent anesthetic gas, cyclopropane (chapter 14), was first used at the University of Wisconsin General Hospital, at Madison, in 1934. Small amounts rapidly produce insensitivity to pain without rendering the patient unconscious. The great drawback is that cyclopropane forms explosive mixtures with air throughout its effective range of concentrations. Special equipment and an experienced anesthetist are required for its use.

Still another anesthetic, called halothane (chapter 15), has been widely used. Like its relative, chloroform, it is nonflammable. It is more potent than chloroform, yet recovery from its effects is rapid.

Modern surgical practice has moved away from the use of a single anesthetic. Generally a patient is given a strong sedative such as thiopental (section 19.9) by injection. This produces unconsciousness. The gaseous anesthetic then administered provides insensitivity to pain and keeps the patient unconscious. A relaxant, such as curare or succinylcholine iodide, may also be employed. These compounds produce complete relaxation; thus, only light anesthesia is required. This avoids the hazards of deep anesthesia.

Incidentally, curare is the arrow poison used by South American Indian tribes. Actually, there are three curares, called tube, pot, or gourd curare, depending on the type of container in which they are stored. These are obtained from different plants. The one used in conjunction with anesthesia is obtained from *Chondrodendron tomentosum*. Large doses of curare kill by causing a complete relaxation of all muscles. Death occurs because of respiratory failure.

Figure 19.10 Coca leaves and illicit forms of cocaine. (Courtesy of the U.S. Bureau of Narcotics and Dangerous Drugs, Washington, D.C.)



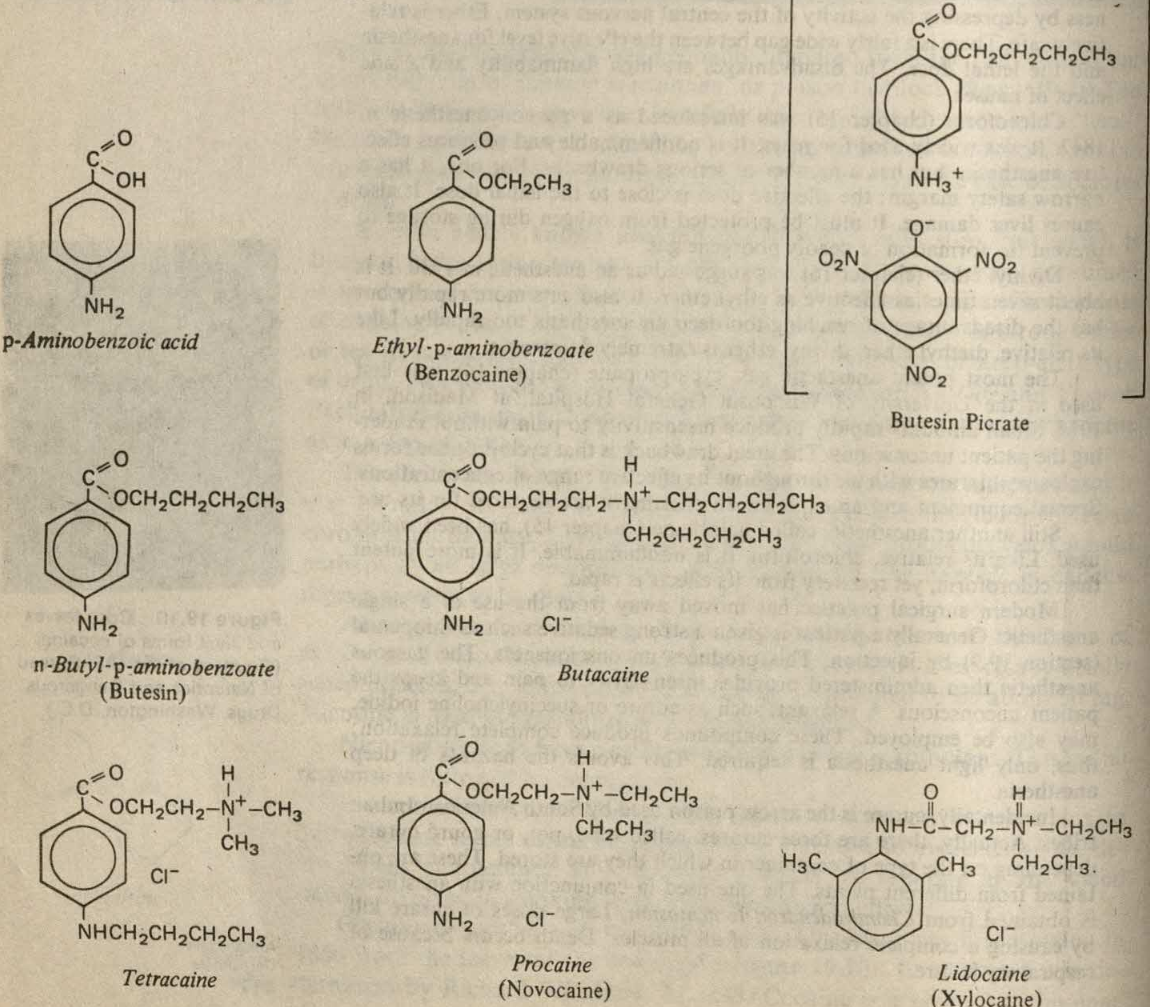
Cocaine

dence and power. It even induces euphoria in some users. These stimulant effects are short-lived (lasting about an hour) and are followed by depression. Overdose or repeated use may lead to paranoia, psychosis, or hallucinations. Overdose may also cause death through heart attack or respiratory arrest.

Cocaine is expensive, which may be the reason for its popularity among some members of the wealthy "jet set" of international socialites. These people usually sniff it up their noses from specially designed spoons. Repeated administrations in this manner lead to a deterioration of the mucous linings of the nose. The snorter is thus rendered more susceptible to infection and disease.

Cocaine was once used as a local anesthetic, the first compound successfully used as such. It is quite toxic, however. Even before Willstätter deter-

Figure 19.11 Some local anesthetics.



p-*Aminobenzoic acid*

Ethyl-p-*aminobenzoate*
(Benzocaine)

Butesin Picrate

n-*Butyl*-p-*aminobenzoate*
(Butesin)

Butacaine

Tetracaine

Procaine
(Novocaine)

Lidocaine
(Xylocaine)

mined the structure of cocaine, the search was under way for synthetic compounds with similar properties.

19.11 Support Your Local Anesthetic

For dental work or minor surgery, it is usually desirable to deaden the pain in a part of the body only. After the initial work with cocaine, several other compounds were found that would carry out that function. For example, certain esters of *p*-aminobenzoic acid act as local anesthetics (**figure 19.11**). The ethyl and *n*-butyl esters are used to relieve the pain of burns and open wounds. These are applied as ointments, usually in the form of picrate salts.

More powerful in their anesthetic action are derivatives in which a second nitrogen atom is incorporated in the alkyl group of the ester. Perhaps the best known of these is procaine (*Novocaine*), first synthesized by Alfred Einhorn in 1905. Procaine can be injected as a local anesthetic. It can also be injected into the spinal column so that it deadens the entire lower portion of the body. Procaine works by blocking nerve impulses to the brain.

Table 19.3
Toxicities of a variety of drugs*

	Drug	*LD_{50} (in milligrams per kilogram of body weight)*	*Method of Administration*	*Experimental Animal*
Local anesthetics	Lidocaine	400	Subcutaneous	Mice
	Procaine	50	Intravenous	Rats
	Cocaine	17.5	Intravenous	Rats
Barbiturates	Barbital	600	Oral	Mice
	Pentobarbital	130	Intraperitoneal	Mice
	Secobarbital	125 (MLD)†	Oral	Rats
	Phenobarbital	660	Oral	Rats
	Amobarbital	575	Oral	Rabbits
	Thiopental	120	Intraperitoneal	Rats
Narcotics	Morphine	500	Subcutaneous	Mice
	Codeine	120 (MLD)	Oral	Guinea pigs
	Heroin	150	Subcutaneous	Rabbits
	Meperidine	170	Oral	Rats
Stimulants	Caffeine	200	Oral	Rats
	Nicotine	55	Oral	Rats
		1.0 (MLD)	Intravenous	Rats
	Amphetamine	5 (MLD)	Oral	Rats
		85	Oral	Rabbits
	Methamphetamine	70	Intraperitoneal	Mice
	Epinephrine	50	Oral	Mice
	Mescaline	500	Intraperitoneal	Mice

*Comparisons of toxicities in different animals—and extrapolation to humans—are at best crude approximations. Method of administration can also have a profound effect on the observed toxicity.

†Minimum lethal dose.

When the block involves the spinal cord, messages of pain are prevented from reaching the brain.

More powerful than procaine (**table 19.3**)—but also more toxic—is the compound butacaine. Another chemical, tetracaine, is used for topical anesthesia of the eyes and for spinal anesthesia. The "local" of choice nowadays is usually lidocaine. This compound is highly effective yet has a fairly low toxicity. Note that lidocaine is not a derivative of *p*-aminobenzoic acid but that it does share some structural features with the other compounds shown in **figure 19.11.**

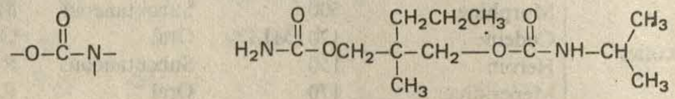
19.12 Chemical Quiet: The Tranquilizers

We will look at one other class of nitrogen-containing compounds before leaving the amine scene. Strictly speaking, not all the tranquilizers are amines; the carbamates are perhaps more closely related to the amides (chapter 18). But the compounds in this section have similar physiological properties and will be grouped together on that basis.

The hectic pace of life in the modern world has driven people to seek rest and relaxation in chemicals. Ethyl alcohol is undoubtedly the most widely used tranquilizer. The drink before dinner—to "unwind" from the tensions of the day—is very much a part of the American way of life. Many people, however, seek their relief in other chemical forms.

Several over-the-counter drugs—*Cope, Vanquish,* and *Compoz,* among others—claim to be able to help us cope with or vanquish our problems or at least to compose ourselves in the face of minor adversity. Such products usually contain a little aspirin plus an antihistamine. The latter has a side effect of making one drowsy. These products have come under attack by consumer groups for being worthless at best—and perhaps even dangerous.

Another group of drugs, available only by prescription, is widely employed to calm nervous tension. Several of these drugs are carbamates, compounds whose functional group resembles both an amide and an ester (**figure 19.12**). Simple derivatives, such as ethyl carbamate, act as mild soporifics (sleep-inducing agents). The best-known tranquilizer in this group is

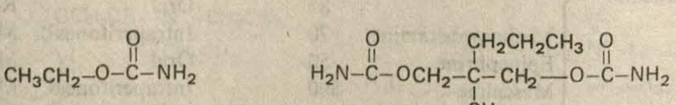


$-O-\overset{O}{\overset{\|}{C}}-\underset{|}{N}-$

$H_2N-\overset{O}{\overset{\|}{C}}-OCH_2-\underset{CH_3}{\overset{CH_2CH_2CH_3}{C}}-CH_2-O-\overset{O}{\overset{\|}{C}}-NH-CH\begin{array}{l}CH_3\\CH_3\end{array}$

The carbamate functional group

Carisoprodol (Soma)



$CH_3CH_2-O-\overset{O}{\overset{\|}{C}}-NH_2$

$H_2N-\overset{O}{\overset{\|}{C}}-OCH_2-\underset{CH_3}{\overset{CH_2CH_2CH_3}{C}}-CH_2-O-\overset{O}{\overset{\|}{C}}-NH_2$

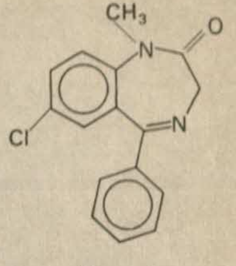
Ethyl carbamate (a mild soporific)

Meprobamate (Equanil, Miltown)

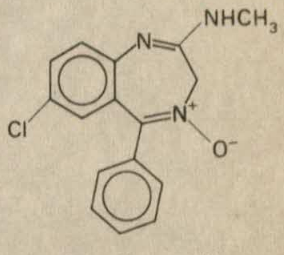
Figure 19.12 Some carbamates.

meprobamate (*Equanil* or *Miltown*). Proceeds from the sale of meprobamate amount to many millions of dollars per year. Another carbamate, carisoprodol (*Soma*), is employed as a muscle relaxant.

Two other widely used antianxiety drugs have seven-membered heterocyclic rings. They are diazepam (*Valium*) and chlordiazepoxide (*Librium*). These benzodiazepine derivatives and the carbamates were formerly called "minor tranquilizers." They are still widely used for treatment of anxiety. Some studies have shown them to be remarkably effective. Others have found the drugs to be little better than a placebo—a pill that looks like the drug tablet but which contains no active ingredient. The actual effect apparently depends upon the expectation of the patient.



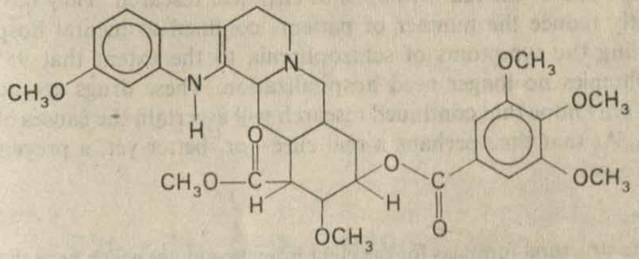
Diazepam
(Valium)



Chlordiazepoxide
(Librium)

For centuries, the people of India used the snakeroot plant, *Rauwolfia serpentina*, to treat a variety of ailments including fever, snakebite, and other poisonings, and—most importantly—to treat maniacal forms of mental illness. Western scientists became interested in the plant near the middle of the 20th century—after disdaining such remedies as quackery for many generations.

In 1952, rauwolfia was introduced into American medical practice as a hypotensive (blood-pressure-reducing) agent by Robert Wilkins, of Massachusetts General Hospital. In the same year, Emil Schlittler, of Switzerland, isolated an active alkaloid which he named reserpine and which has the following impressive (intimidating?) structure.



Reserpine

Rauwolfia was found not only to reduce blood pressure but also to bring about sedation. The latter finding attracted the interest of psychiatrists, who found reserpine so effective that by 1953 it had replaced electroshock therapy for 90% of their psychotic patients.

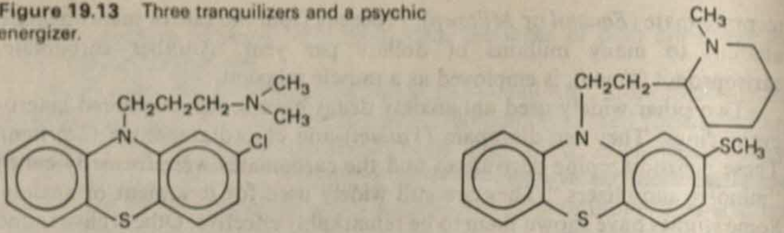
Also in 1952, chlorpromazine (*Thorazine*), which had been used in France as an antihistamine, was tried on psychotic patients in the United States as a tranquilizer. It was found to be extremely effective against the symptoms of schizophrenia.

Many compounds related to chlorpromazine have been synthesized. Several of these have been found to have interesting physiological properties. Promazine itself is a tranquilizer, but not as potent a one as chlorpromazine.

Thioridazine (*Mellaril*) is a potent tranquilizer, reputed to be without some of the undesirable side effects of chlorpromazine.

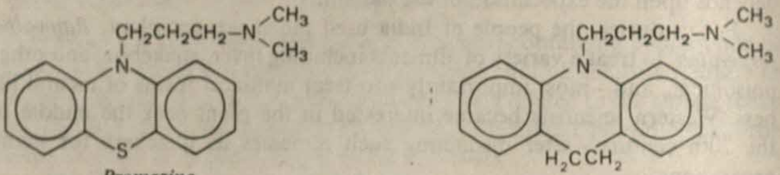
It is worth noting that imipramine, which differs from promazine only in that the sulfur atom is replaced by a $—CH_2CH_2—$ group, is not a tran-

Figure 19.13 Three tranquilizers and a psychic energizer.



Chlorpromazine
(Thorazine)

Thioridazine
(Mellaril)



Promazine

Imipramine

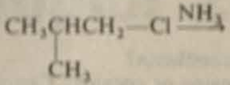
quilizer at all. Instead, it is a psychic energizer. This indicates that slight structural changes sometimes can result in profound changes in properties and that we have a long way to go in understanding why drugs act as they do.

The antipsychotic drugs—reserpine and the promazine derivatives—have been one of the real triumphs of chemical research. They have served to greatly reduce the number of patients confined to mental hospitals by controlling the symptoms of schizophrenia to the extent that 95% of all schizophrenics no longer need hospitalization. These drugs are not cures. We can only hope that continued research will ascertain the causes of schizophrenia. At that time perhaps a real cure—or, better yet, a preventative—can be found.

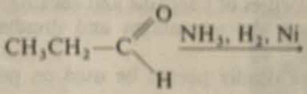
Problems

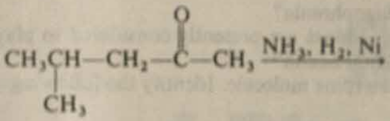
1. Write structural formulas for the eight isomeric amines which have the molecular formula $C_4H_{11}N$. Give each a common name and classify it as a primary, secondary, or tertiary amine.
2. Distinguish between a carbocyclic compound and a heterocyclic compound.
3. Write structural formulas for the following.
   - a. dimethylamine
   - b. 3-aminopentane
   - c. cyclohexylamine
   - d. 1,6-diaminohexane
   - e. aniline
   - f. *m*-bromoaniline
   - g. N,N-dimethylaniline
   - h. 2-aminoethanol
   - i. diethylmethylamine
   - j. α-aminobutyric acid
   - k. pyridine
   - l. purine
   - m. pyrimidine
   - n. "aniline hydrochloride"
   - o. anilinium bromide
   - p. tetramethylammonium chloride
4. What is an alkaloid?
5. Which member of each pair has the higher boiling point? Why?
   - a. *n*-butylamine and *n*-pentane
   - b. *n*-butylamine and *n*-butyl alcohol
   - c. trimethylamine and *n*-propylamine
6. An amine is insoluble in water, yet it dissolves readily in aqueous hydrochloric acid. Explain.

7. Draw the structural formula of and name the amine formed in each of these reactions.

a. 

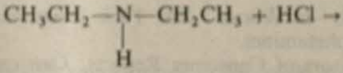
$CH_3\underset{\displaystyle \overset{|}{CH_3}}{CH}CH_2{-}Cl \xrightarrow{NH_3}$

b. 

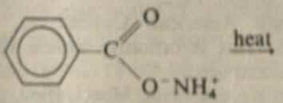
c. 

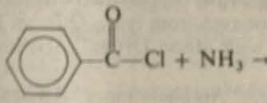
$CH_3\underset{\displaystyle \overset{|}{CH_3}}{CH}{-}CH_2{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}CH_3 \xrightarrow{NH_3,\ H_2,\ Ni}$

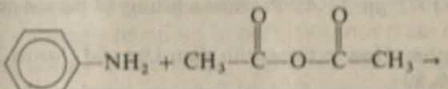
8. Draw the structural formula for the principal organic product of each of these reactions.

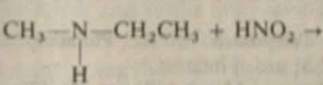
a. 

$CH_3CH_2{-}\underset{\displaystyle \overset{|}{H}}{N}{-}CH_2CH_3 + HCl \rightarrow$

b. 

c. 

d. 

e. 

$CH_3{-}\underset{\displaystyle \overset{|}{H}}{N}{-}CH_2CH_3 + HNO_2 \rightarrow$

9. Why are nitrate and nitrite food additives considered by some people to be health hazards?

10. Which of these drugs are single chemical compounds? Which are mixtures?

a. opium
b. morphine
c. phenobarbital
d. chlorpromazine
e. rauwolfia
f. reserpine
g. *Benzedrine* (amphetamine)
h. *Dexedrine* (dextro amphetamine)

11. Is caffeine addictive? Is nicotine?

12. Why do you think nicotine is so much more toxic when injected intravenously than when taken orally?

13. If the minimum lethal dose of amphetamine is 5 mg per kilogram of body weight what would be the MLD for a 70-kg person? Can toxicity studies on animals always be extrapolated to humans?

14. What is the basic structure common to all barbiturate molecules? How is the basic structure modified to change the properties of individual barbiturate drugs?
15. What is synergism?
16. How do local anesthetics work? What is spinal anesthesia?
17. Refer to **table 19.3.** Which is more toxic—procaine or cocaine? Can you use the data in **table 19.3** to compare the toxicities of lidocaine and cocaine?
18. List three general anesthetics. What are the advantages and disadvantages of each?
19. How does curare kill? How can such a deadly poison be used on people in surgery without killing them?
20. Are tranquilizers a cure for schizophrenia?
21. Which two naturally occurring amines are presently considered to play major roles in the biochemistry of mental health?
22. Examine the structure of the reserpine molecule. Identify the following.
    a. five ether functions
    b. two amine functions
    c. two ester functions

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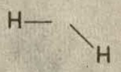
chapter 20

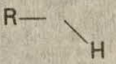
Compounds of Sulfur and Phosphorus

Organic compounds containing sulfur and phosphorus make life possible. They also make life unpleasant (as when skunk and nature lover meet) or even unlivable (as when some chemical warfare agents are put to use). This enormous range of effects makes organic sulfur and phosphorus compounds extremely interesting to people studying the chemistry of life. We now know, for example, that sulfur atoms in protein molecules play a major role in determining the shapes of these compounds. And the shapes of proteins, particularly enzymes, are critical to their function. Without active enzyme catalysts, biochemical reactions would not be fast or specific enough to sustain life. Organophosphorus compounds are involved in many of the energy-releasing reactions in cells. Without these compounds, the engines we call our bodies would simply run down for lack of power.

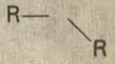
As is our habit, we shall look at some of the simple organic compounds of phosphorus and sulfur first, saving for subsequent chapters our consideration of the more complex compounds so vital to living cells. It might be worth mentioning that the "subsequent chapters" to which we so often refer are almost upon us.



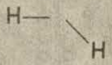
Water



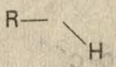
An alcohol



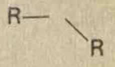
An ether



Hydrogen sulfide



A thiol



A thioether

20.1 Thiols: Skunks and Scholars

Alcohols and ethers can be considered to be derived from water by replacement of one or both of its hydrogen atoms by alkyl groups. Some classes of sulfur-containing compounds can be derived from hydrogen sulfide in a similar way. The prefix *thio-* indicates the substitution of a sulfur atom for an oxygen atom in a compound. If ROH is an alcohol, RSH is a *thio*alcohol, or *thiol.*

The functional group (—SH) is called a *sulfhydryl group* (it contains sulfur and hydrogen). For many years the thiols were called *mercaptans,* a name which was derived from their ability to react with mercury (from the

Latin *mercurium captans*, literally, "seizing mercury"). You may still encounter the name, though chemists seldom use it anymore.

The thiols are named in the same way that the alcohols are, except that in the IUPAC system the *-ol* becomes *-thiol* and the final *-e* of the parent hydrocarbon name is retained. Thus, it is butanol but butan*e*thiol. In the common system, *alcohol* is replaced by *mercaptan*.

$CH_3CH_2CH_2CH_2OH$

1-Butanol
(n-butyl alcohol)

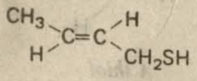
$CH_3CH_2CH_2CH_2SH$

1-Butanethiol
(n-butyl mercaptan)

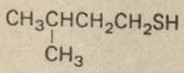
Unlike oxygen, sulfur cannot participate in hydrogen bonding. Thus, the thiols have lower boiling points than the corresponding alcohols, even though they have greater molecular weights. Thiols do not hydrogen bond to water, either, and hence are much less soluble in water than alcohols with the same number of carbon atoms.

Perhaps the most notable and noticeable property of thiols is their offensive odor. The unforgettable odor of a skunk is due to two thiols and a compound called a disulfide (**figure 20.1**). It is of interest that for three-quarters of a century textbooks confidently stated that the defense odor of a skunk was due to *n*-butyl mercaptan (1-butanethiol). In 1974, however, two chemists at the University of New Hampshire proved that the odor was composed of the three major components shown in **figure 20.1.** Kenneth Andersen and David Bernstein found no 1-butanethiol in "skunk oil." (Moral: even the "facts" of chemistry sometimes change.)

Figure 20.1 The odor of a skunk is made up of three sulfur compounds. *trans*-2-Butene-1-thiol accounts for about 40% of that odor. 3-Methyl-1-butanethiol and methyl-1-(*trans*-2-butenyl) disulfide account for about 30% each. (Photo by John Gerard.)

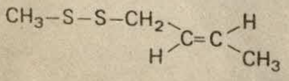


trans-*2-Butene-1-thiol*



$CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2SH$

3-Methyl-1-butanethiol



*Methyl-1-(*trans*-2-butenyl)disulfide*

Foul odors aren't all bad, however. Small amounts of thiols are added to natural gas in order that leaks of the otherwise odorless gas can be detected by smell. Someone who says, "I smell gas," is actually smelling the thiol in the gas mixture. Low concentrations of thiols may contribute desirable qualities to flavors and odors. Oysters and cheddar cheese contain small amounts of methanethiol. The onion is made piquant by the presence of 1-propanethiol (**figure 20.2**). It is also true that not all thiols stink. Odor decreases with increasing molecular weight. With 10 or more carbon atoms per molecule, the odor may be pleasant.

The thiols of low molecular weight are somewhat toxic. Their foul odors, however, make it possible for us to detect levels much lower than those that are dangerous. For example, our noses can detect 0.02 ppb (by volume) of ethanethiol in air. The obnoxious odor would cause almost anyone to flee long before toxic levels were reached.

20.2 Chemical Properties of the Thiols

Perhaps the most important chemical property of thiols for us living things is the fact that the thiols form insoluble compounds with heavy metal ions such as those of mercury and lead.

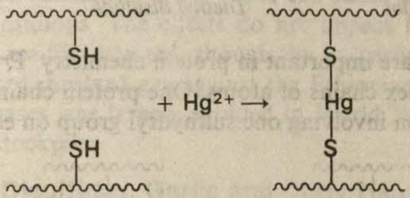
Table 20.1
A comparison of the physical properties of an alcohol and a thiol

Compound	*Formula*	*Molecular Weight*	*Boiling Point (in degrees Celsius)*	*Solubility (in grams per 100 g of water)*
Ethanol	CH_3CH_2OH	46	78	∞
Ethanethiol	CH_3CH_2SH	62	37	1.5

$$2\ \mathrm{RSH} + \mathrm{Hg}^{2+} \longrightarrow \mathrm{RS{-}Hg{-}SR} + 2\ \mathrm{H}^{+}$$

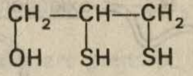
$$2\ \mathrm{RSH} + \mathrm{Pb}^{2+} \longrightarrow \mathrm{RS{-}Pb{-}SR} + 2\ \mathrm{H}^{+}$$

Most enzymes have amino acids with sulfhydryl groups at or near the active sites. Heavy metal ions tie up these groups, rendering the enzyme inactive.



It is this loss of enzyme activity that ultimately leads to the various symptoms of lead or mercury poisoning.

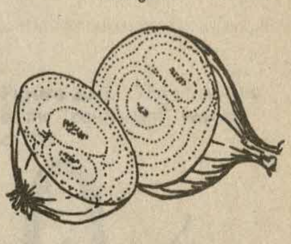
The antidote for mercury poisoning also contains sulfhydryl groups. British scientists, searching for an antidote for the arsenic-containing war gas, Lewisite, came up with a compound effective for heavy metal poisoning as well. The compound, a dithio analog of glycerol (chapter 16), came to be known as BAL (British Anti-Lewisite).



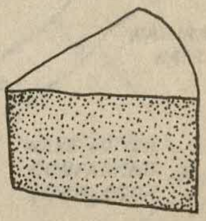
$$\underset{\mathrm{OH}}{\mathrm{CH_2}}{-}\underset{\mathrm{SH}}{\mathrm{CH}}{-}\underset{\mathrm{SH}}{\mathrm{CH_2}}$$

BAL acts by picking up the mercury between the sulfhydryl groups in a sort of pincer action.

CH_3SH

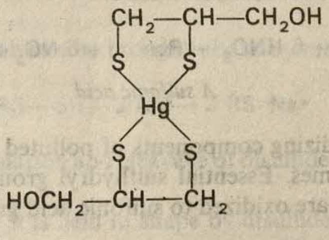


$CH_3CH_2CH_2SH$



CH_3SH

Figure 20.2 Oysters, onions, and cheddar cheese owe their flavors in part to thiols.



The BAL is said to chelate (from the Greek *chela,* "claw") the metal ion. Thus tied up, the mercury cannot attack the vital enzymes.

Now the bad news. The symptoms of mercury poisoning may not show up for several weeks. By the time the symptoms—loss of equilibrium, sight, feeling, hearing—are recognizable, extensive damage has already been done to the brain and nervous system. Such damage is largely irreversible. The BAL antidote is effective only when a person knows that poison has been ingested and seeks treatment right away.

Thiols are readily oxidized. Mild oxidizing agents bring about the removal of two hydrogen atoms from two thiol molecules. The remaining pieces of the thiols combine to form a new molecule, called a disulfide, with a covalent bond between two sulfur atoms.

$$R{-}S{-}\boxed{H\ H}{-}S{-}R + I_2 \longrightarrow RS{-}SR + 2\,HI$$

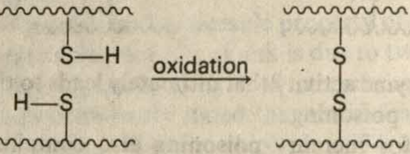
A disulfide

$$2\,RSH + H_2O_2 \longrightarrow RS{-}SR + 2\,H_2O$$

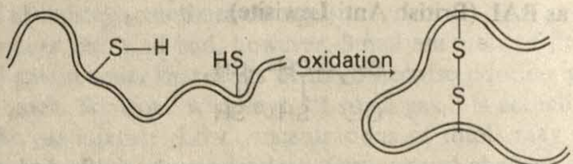
$$2\,CH_3CH_2SH + I_2 \longrightarrow CH_3CH_2S{-}SCH_2CH_3 + 2\,HI$$

Ethanethiol *Diethyl disulfide*

Such mild oxidations are important in protein chemistry. Protein molecules consist of long, complex chains of atoms. One protein chain may be joined to another by oxidation involving one sulfhydryl group on each chain.



Or a loop may be formed in a single chain when two well-separated sulfhydryl groups are oxidized.

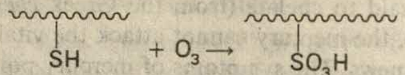


One practical application of this reaction is discussed in section 20.4. Strong oxidation of thiols produces *sulfonic acids.*

$$RSH + 6\,HNO_3 \longrightarrow RSO_3H + 6\,NO_2 + 3\,H_2O$$

A sulfonic acid

Ozone and other oxidizing components of polluted air probably act in part by deactivating enzymes. Essential sulfhydryl groups at the active site on the enzyme molecule are oxidized to sulfonic acid groups.



Active enzyme *Inactive enzyme*

20.3 Thioethers: Mustard Gas

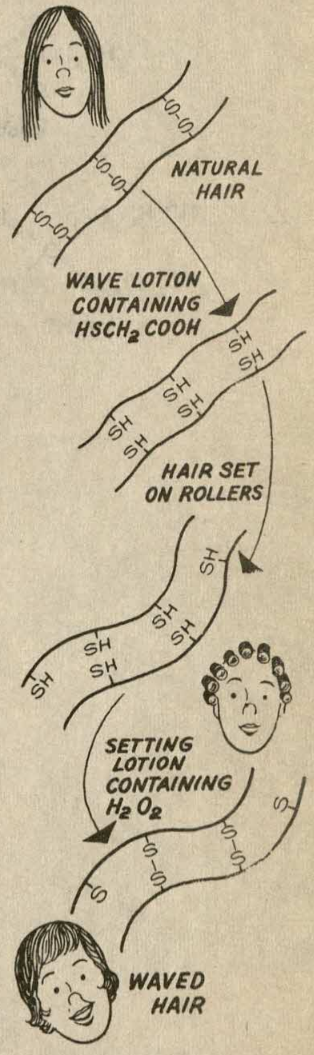
The sulfur analogs of the ethers are called thioethers or, alternatively, dialkyl sulfides. (Note that dialkyl sulfides are not the same as the disulfides mentioned in section 20.2.) The thioethers have unpleasant odors, though generally not as bad as those of the thiols. They have low boiling points and are essentially insoluble in water. Dimethyl sulfide (CH_3SCH_3) is used as an odorant in natural gas.

During World War I, a dichloro derivative of diethyl sulfide, bis(2-chloroethyl) sulfide (mustard gas), received notoriety as a poisonous war gas. The compound is not a gas at all but an oily liquid which boils at 217 °C. Contact with either the liquid or its vapor causes blisters which are painful and slow to heal. Inhalation of the vapor can cause death. The action of the compound is insidious. The effects do not appear for several hours after exposure. It is readily detected, though, by its garlic or horseradish odor. The Italians used mustard gas against the Ethiopians in 1936, but the use of poisonous gases was largely avoided in World War II despite the existence of huge stockpiles.

$ClCH_2CH_2—S—CH_2CH_2Cl$

bis (2-Chloroethyl) sulfide
("mustard gas")

Figure 20.3 The chemistry of the "permanent" waving of hair.



20.4 Dialkyl Disulfides: Garlic and Curly Hair

The dialkyl disulfides do have counterparts among the oxygen-containing families of organic compounds, but we did not include these oxygen analogs in our previous studies. The critical importance of the disulfide bond in protein chemistry, however, makes consideration of dialkyl disulfides imperative.

Dialkyl disulfides are prepared by the cautious oxidation of thiols (section 20.2). One disulfide that is well known, by odor if not by name, is diallyl disulfide, the principal constituent of oil of garlic.

$$CH_2{=}CH—CH_2—S—S—CH_2—CH{=}CH_2$$

The reaction in which disulfides are prepared from thiols can be reversed. The reversal involves reductive cleavage of the sulfur-sulfur bond. For simple disulfides, this reduction can be accomplished by zinc and sulfuric acid.

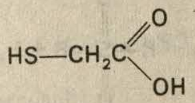
$$RS—SR + Zn + H_2SO_4(aq) \longrightarrow 2\ RSH + ZnSO_4(aq)$$

Alternatively, the scission can be brought about by metallic sodium.

$$RS—SR + 2\ Na \longrightarrow 2\ RS^-Na^+$$

In living organisms, formation and cleavage of disulfide linkages are catalyzed by enzymes.

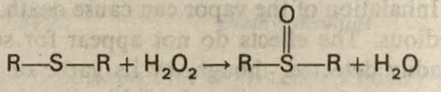
Hair is protein, and it is held in shape by disulfide linkages between adjacent protein chains. The "permanent" waving of hair (**figure 20.3**) involves the use of a lotion containing a reducing agent such as thioglycolic acid.



This wave lotion ruptures the disulfide linkages of the hair protein. The hair is then set on curlers or rollers and is treated with a mild oxidizing agent such as hydrogen peroxide (H_2O_2). Disulfide linkages are formed in new positions to give new shape to the hair. Exactly the same chemical process can be used to straighten naturally curly hair. The change in hair style depends only on how one arranges the hair after the disulfide bonds have been reduced and before reoxidation takes place.

20.5 Sulfoxides: DMSO, Solvent and Drug

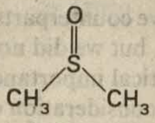
Mild oxidation of thioethers produces compounds called *sulfoxides.*



$$R{-}S{-}R + H_2O_2 \longrightarrow R{-}\overset{\overset{\displaystyle O}{\|}}{S}{-}R + H_2O$$

A sulfoxide

The simplest, and by far most important, sulfoxide is dimethyl sulfoxide (DMSO).

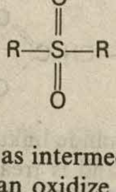


This compound is a highly polar liquid which freezes at 18 °C and boils at 189 °C. It is soluble in most organic solvents but readily dissolves in water also. The latter solubility is due to hydrogen bonding of the DMSO oxygen with the hydrogens of water.

DMSO has a variety of interesting physiological properties. It not only penetrates skin and tissues readily but can carry along other drugs into the tissues. DMSO itself seems to act as an analgesic and antiinflammatory agent. It has been reported to provide relief from sprains and bruises, arthritis, burns, headaches, and other afflictions. Some problems with toxicity in laboratory animals led the Food and Drug Administration to call for an end to clinical testing of DMSO in 1965. Reevaluation of the data and clinical experience in other countries have shown that toxicity to humans may have been overestimated. The FDA has since relaxed its ban. DMSO may yet become a most useful drug.

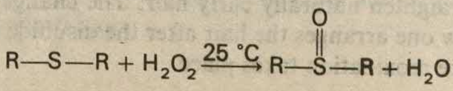
20.6 Sulfones: Solvents and Sleep Inducers

The mild oxidation of thioethers produces sulfoxides, compounds in which one oxygen atom is attached to sulfur. Vigorous oxidation of thioethers yields *sulfones,* compounds with two oxygens attached to sulfur.

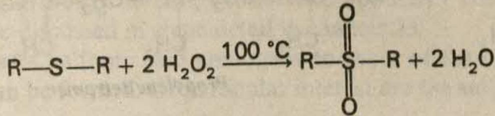


$$R{-}\underset{\underset{\displaystyle O}{\|}}{\overset{\overset{\displaystyle O}{\|}}{S}}{-}R$$

Sulfoxides are probably formed as intermediates in this process. Indeed, by using hydrogen peroxide, one can oxidize a thioether to either a sulfoxide or a sulfone, depending on the temperature and molar ratio.

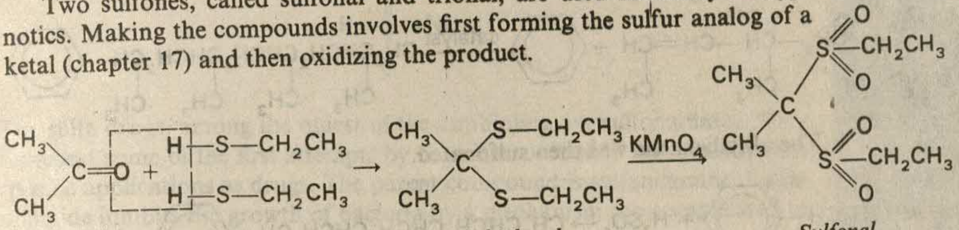


$$R{-}S{-}R + H_2O_2 \xrightarrow{25\ ^\circ C} R{-}\overset{\overset{\displaystyle O}{\|}}{S}{-}R + H_2O$$

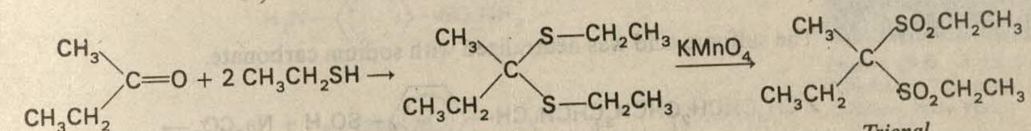


$$R{-}S{-}R + 2\,H_2O_2 \xrightarrow{100\ ^\circ C} R{-}SO_2{-}R + 2\,H_2O$$

Two sulfones, called sulfonal and trional, are used medically as hypnotics. Making the compounds involves first forming the sulfur analog of a ketal (chapter 17) and then oxidizing the product.



Acetone *Ethanethiol* *A thioketal* *Sulfonal*



Trional

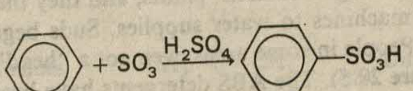
Ethyl methyl ketone

20.7 Sulfonic Acids and Their Derivatives

In section 20.2 we saw that strong oxidation of thiols gives sulfonic acids.

$$RSH + 6\,HNO_3 \rightarrow RSO_3H + 6\,NO_2 + 3\,H_2O$$

Aromatic sulfonic acids can be made by direct sulfonation of arenes. For example, benzene reacts with fuming sulfuric acid (H_2SO_4 containing excess SO_3) to form benzenesulfonic acid.



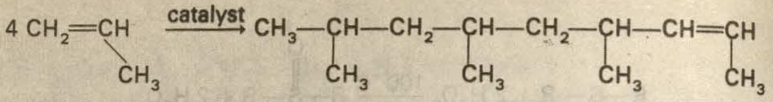
The sulfonic acids are strong acids, essentially completely ionized in aqueous solution.

$$RSO_3H + H_2O \rightarrow RSO_3^- + H_3O^+$$

They react with bases to form salts.

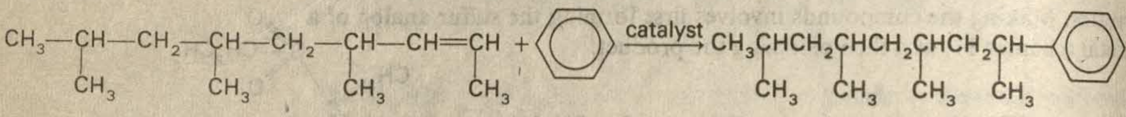
$$RSO_3H + NaOH(aq) \rightarrow RSO_3^-Na^+(aq) + H_2O$$

Modern synthetic detergents are often sodium salts of sulfonic acids. The first economically successful synthetic detergents were made from propylene, benzene, sulfuric acid, and sodium carbonate. Propylene was condensed into a tetramer (*tetra,* "four," and *mer,* "part").

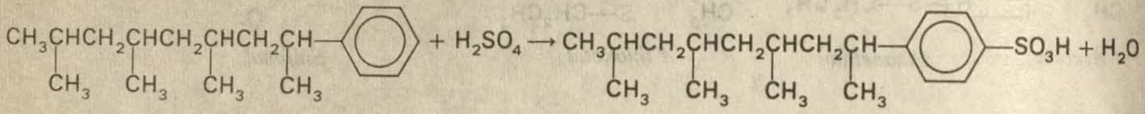


Propylene *Propylene tetramer*

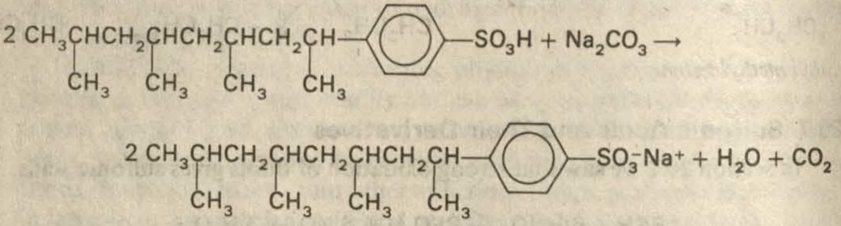
The reaction of the tetramer with benzene formed an alkylbenzene.



The alkylbenzene was then sulfonated.



The sulfonic acid was neutralized with sodium carbonate.



ABS

The final product, called an alkylbenzenesulfonate, or ABS, detergent did an excellent job of cleaning, even in hard water. But ABS detergents were not broken down in sewage treatment plants, and they therefore made their way from washing machines to water supplies. Suds began to pile high in rivers (**figure 20.4**). People in some areas even got a "head" of foam on their drinking water (**figure 20.5**). The ABS detergents have been largely replaced by degradable linear alkylsulfonate (LAS) detergents.

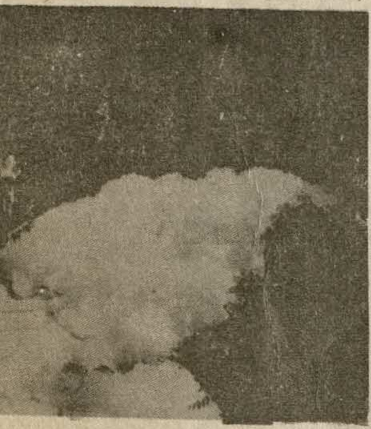
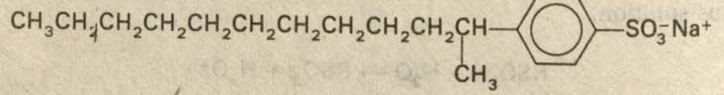


Figure 20.4 Foaming rivers were quite common in the early 1960s. This problem was solved by the development of biodegradable detergents. (Courtesy of the U.S. Department of Agriculture, Washington, D.C.)

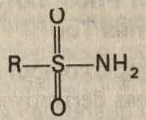


LAS

Microorganisms can break down the LAS molecules through the action of enzymes which catalyze the degradation of the molecule two (and *only* two) carbons at a time. The branched chain in ABS molecules blocks the enzyme action, preventing degradation.

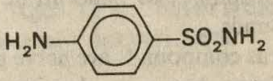
The cleansing action of detergents is quite similar to that of soap. (*Soap* and *detergent* are used almost interchangeably by the public, but the terms refer to different, though similar, chemical compounds.) The mechanism of cleaning will be discussed in some detail in chapter 23.

Derivatives of sulfonic acid analogous to those of the carboxylic acids (chapter 18) can be formed. Of particular interest are the sulfonamides.



$$R-\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}-NH_2$$

The sulfa drugs, among the oldest of the antibiotics, are sulfonamides. They represent some of the first attempts by chemists to "build" compounds with specific applications as drugs. The parent compound is sulfanilamide. Sulfanilamide inhibits the growth of bacteria by a mechanism too complicated to be detailed here.



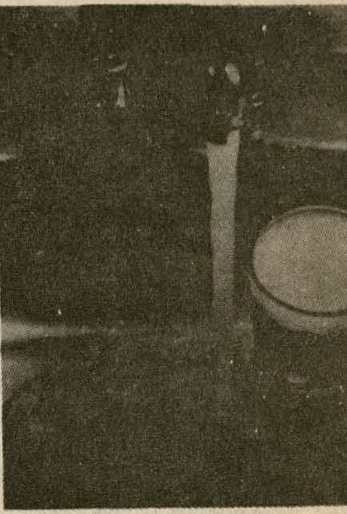
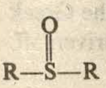
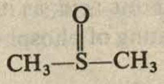
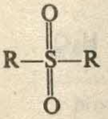
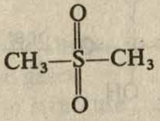
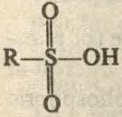
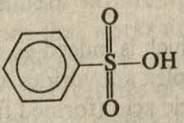
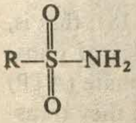
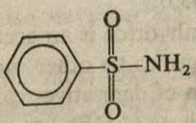
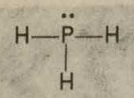


Figure 20.5 A glass of suds. (Courtesy of Bergwall Productions, New York.)

Table 20.2
Some families of sulfur-containing organic compounds

Functional Group	*Family Name*	*Example*	*Compound Name*
R—S—H	Thiols (mercaptans)	CH_3SH	Methanethiol (methyl mercaptan)
R—S—R	Thioethers (sulfides)	$CH_3—S—CH_3$	Dimethyl sulfide
R—S—S—R	Disulfides	$CH_3—S—S—CH_3$	Dimethyl disulfide
 $R-\overset{O}{\overset{\|}{S}}-R$	Sulfoxides	 $CH_3-\overset{O}{\overset{\|}{S}}-CH_3$	Dimethyl sulfoxide
 $R-\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}-R$	Sulfones	 $CH_3-\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}-CH_3$	Dimethyl sulfone
 $R-\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}-OH$	Sulfonic acids		Benzenesulfonic acid
 $R-\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}-NH_2$	Sulfonamides		Benzenesulfonamide

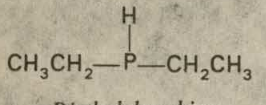


$$\mathrm{H{-}\underset{\underset{H}{|}}{\overset{\cdot\cdot}{P}}{-}H}$$

Phosphine

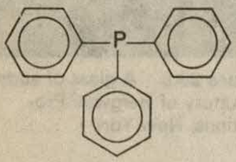
CH_3PH_2

Methylphosphine (primary)

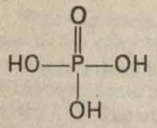


$$\mathrm{CH_3CH_2{-}\overset{\overset{H}{|}}{P}{-}CH_2CH_3}$$

Diethylphosphine (secondary)

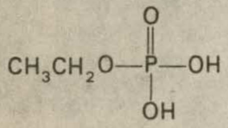


Triphenylphosphine (tertiary)



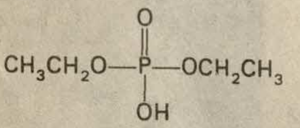
$$\mathrm{HO{-}\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{P}}{-}OH}$$

Phosphoric acid



$$\mathrm{CH_3CH_2O{-}\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{P}}{-}OH}$$

Ethyl dihydrogen phosphate



$$\mathrm{CH_3CH_2O{-}\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{P}}{-}OCH_2CH_3}$$

Diethyl hydrogen phosphate

The pace of our trip through organosulfur chemistry may have left you a little breathless. A summary of the classes of compounds we have discussed is therefore offered in **table 20.2.**

20.8 We're Prosperous with Phosphorus . . . and Poisoned Sometimes Too

Just as sulfur forms some organic compounds analogous to those of oxygen (section 20.1), phosphorus has derivatives analogous to those of nitrogen. We considered the amines (chapter 19) to be derivatives of ammonia; a similar series of phosphorus compounds is derived from the phosphorus analog of ammonia, phosphine. Like the amines, the organic phosphines can be primary, secondary, or tertiary.

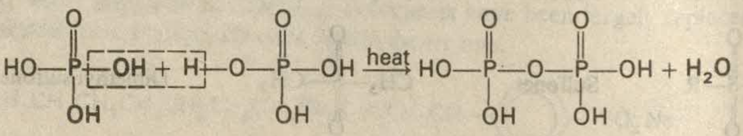
High toxicity is a property alkyl phosphines have in common with a number of other organophosphorus compounds. We shall forego further consideration of the alkyl phosphines to concentrate instead on these other organophosphorus compounds.

Some organophosphorus compounds are nerve poisons, among the most toxic substances known. Some, however, play more positive roles in living systems. The latter are organic derivatives of phosphoric acid rather than of phosphine.

20.9 Esters and Anhydrides of Phosphoric Acid

Of particular importance in the chemistry of living cells are the reactions of phosphate esters and anhydrides. Phosphoric acid is triprotic and may form mono-, di-, and tri- alkyl esters. Esters of phosphoric acid are comparable to esters of carboxylic acids: one hydrogen (or more) is replaced by an alykl group.

Before carbohydrates, such as the sugar fructose, can be metabolized, they must be converted to their phosphate esters (chapter 30). Derivatives of two anhydrides of phosphoric acid are involved in the chemistry of such transformations. Pyrophosphoric acid, as its name suggests (from the Greek *pyr,* "fire"), is formed by heating of phosphoric acid until water is driven off.

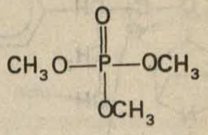


$$\mathrm{HO{-}\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{P}}\boxed{-OH + H}{-}O{-}\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{P}}{-}OH \xrightarrow{heat} HO{-}\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{P}}{-}O{-}\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{P}}{-}OH + H_2O}$$

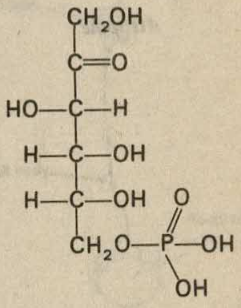
Pyrophosphoric acid

Pyrophosphoric acid, which is indeed an acid, is also an anhydride (of phosphoric acid). More complex anhydrides are possible; the other of interest at this point is triphosphoric acid (formed from three molecules of phosphoric acid and shown on p. 435).

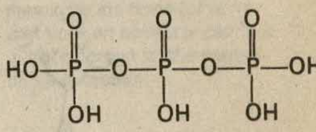
Recall that acetic anhydride is an acetylating agent (chapter 18); that is, it transfers the acetyl group to other molecules. The anhydrides of phosphoric acid, in the form of derivatives called adenosine triphosphate (ATP) and adenosine diphosphate (ADP), are phosphorylating agents; they transfer phosphate groups to molecules, such as the sugars, which can then be metabolized. We will discuss these important reactions in later chapters.



Trimethyl phosphate



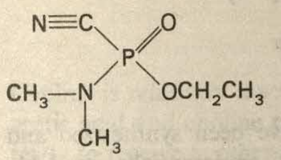
Fructose 6-phosphate



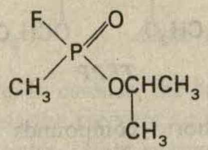
Triphosphoric acid

20.10 Nerve Poisons: War "Gases" and Insecticides

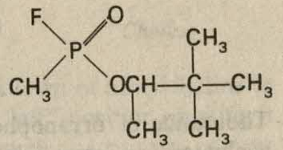
While doing research on organic phosphates as possible insecticides during World War II, German scientists discovered some extremely toxic compounds with frightening potential for use in warfare. The Russians captured a plant which manufactured a compound called Tabun (designated as Agent GA by the U.S. Army). The Soviets dismantled the factory and moved it to Russia. The U.S. Army captured some of the stock, however. Presumably, the gas has since been produced and stocked by both of the former allies. The United States has developed other nerve poisons. One is called Sarin (Agent GB). Sarin is four times as toxic as Tabun. It also has the "advantage" of being odorless (Tabun has a fruity odor). Another organophosphorus nerve poison is Soman (Agent GD). Soman is moderately persistent, whereas Tabun and Sarin are generally nonpersistent.



Tabun

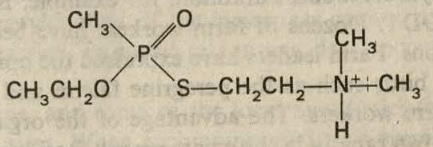


Sarin



Soman

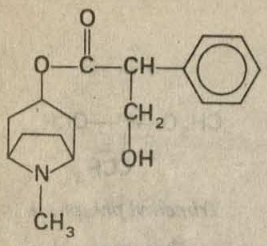
Still another nerve gas is Agent VX. The name and structure of VX have not been released, but it is presumed to be a salt of the cation



Agent VX is less volatile—a little slower to react and therefore a lot more persistent—than the other nerve gases.

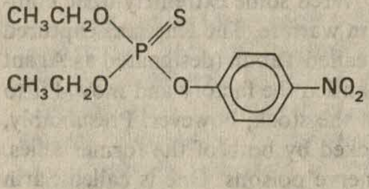
Notice again the variation in structure from one compound to the next. The approach to developing chemical warfare agents is much the same as that for developing drugs—find one that works and then synthesize and test structural variations. These compounds are neither phosphines nor phosphates, but they have some structural features of both types of compounds. Like the phosphines, they have carbon connected directly to phosphorus. And like the phosphates they also have carbon bonded to oxygen in an ester link.

The nerve gases are among the most toxic chemicals known. They kill by inhalation or by absorption through the skin. They result in the complete loss of muscular coordination and subsequent death by cessation of breathing. The usual antidote is atropine injection and artificial respiration. Without this antidote death can occur within 10 minutes.

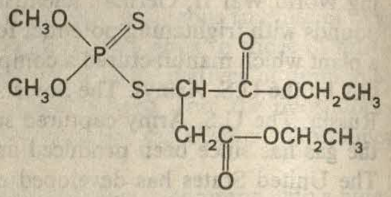


Atropine

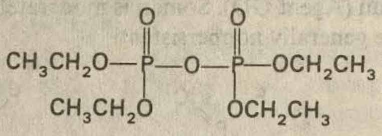
A variety of compounds related to the phosphates have been developed for use as pesticides. With the widespread banning of DDT, these compounds have moved to the forefront in importance. Three widely used ones are malathion, parathion, and tetraethylpyrophosphate (TEPP).



Parathion



Malathion



$(CH_3CH_2O)_2P(=O)-O-P(=O)(OCH_2CH_3)_2$

TEPP

Thousands of organophosphorus compounds have been synthesized and evaluated for insecticidal activity. As many as 26 commercially available organic phosphates have been extensively studied and evaluated for effectiveness against insects and for toxicity in people, laboratory animals, and farm animals (reference 2).

The organic phosphates are generally much more toxic to mammals than the chlorinated hydrocarbons. Parathion, for example, is over 20 times as toxic to rats as DDT. Dozens of farm workers have been killed by these more potent poisons. Farm leaders have expressed the opinion that we have gained safety for birds such as the peregrine falcon and brown pelican at the expense of farm workers. The advantage of the organic phosphates is that they break down rapidly in the environment. Residues of organic phosphates, unlike those of DDT, are seldom found in food.

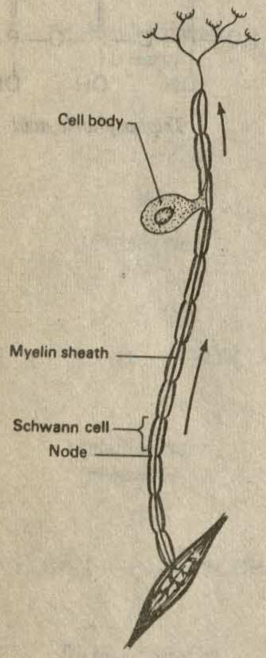


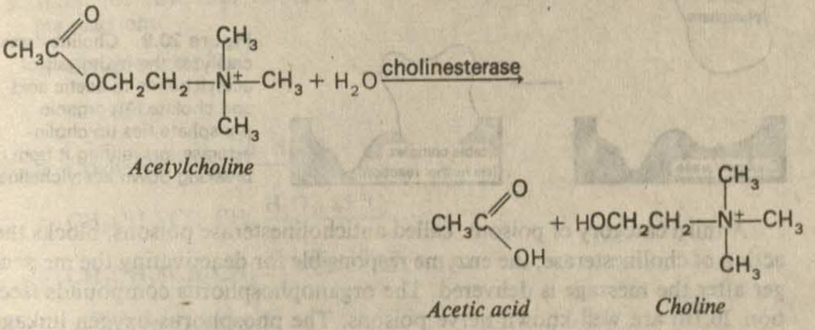
Figure 20.6 A human nerve cell. (After Keeton, William T., *Elements of Biological Science,* New York: W. W. Norton, 1967.)

20.11 The Chemistry of the Nervous System

Some poisons—including the most toxic substances known—act only upon the nervous system. In order to understand how these nerve poisons work, we should take a look at nerve cells and how they work. The nervous system is made up of about 10 billion nerve cells. These vary a great deal in shape and size (**figure 20.6**). The essential parts of each cell are the cell body, the axon, and the dendrites. We will discuss here only those nerves which make up the involuntary (autonomic) nervous system. These carry messages between the organs and glands that act involuntarily (such as the heart, digestive organs, lungs, and so on) and the brain and spinal column.

Although the axons on a given nerve cell may be up to 60 cm (about 2 ft) long, there is no continuous pathway from an organ to the central nervous system. Messages must be transmitted across tiny fluid-filled gaps or synapses (**figure 20.7**). When an electrical signal from the brain reaches the end of an axon, chemicals are liberated that carry impulses across the synapse to the next cell. One such chemical is *acetylcholine*. It is thought to activate the next cell by changing the permeability of the cell membrane, perhaps allowing ions to flow through the membrane more readily.

Once acetylcholine has carried the impulse across the synapse, it is rapidly hydrolyzed to acetic acid and choline. This reaction is catalyzed by an enzyme called *cholinesterase*.



$$CH_3C(=O)OCH_2CH_2-\overset{CH_3}{\underset{CH_3}{N^{\pm}}}-CH_3 + H_2O \xrightarrow{\text{cholinesterase}} CH_3C(=O)OH + HOCH_2CH_2-\overset{CH_3}{\underset{CH_3}{N^{\pm}}}-CH_3$$

Acetylcholine

Acetic acid

Choline

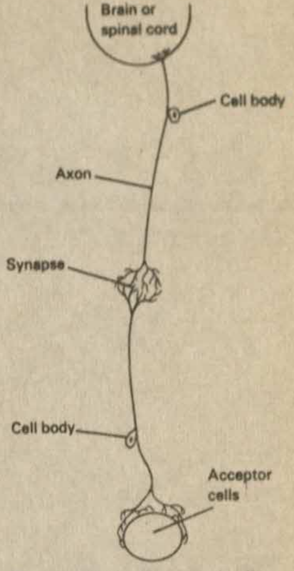


Figure 20.7 Schematic diagram of the pathway by which messages are transmitted to and from an acceptor cell in a gland or organ to the central nervous system.

Choline is relatively inactive. In essence, the breakdown of acetylcholine to acetic acid and choline resets the receptor to the "off" position, making it ready to receive another impulse. Other enzymes, such as acetylase, convert the acetic acid and choline back to acetylcholine, completing the cycle (**figure 20.8**).

Various chemical substances can disrupt the acetylcholine cycle at different points. Botulinus, the deadly toxin given off by *Clostridium botulinum*, an anaerobic bacterium found in improperly processed canned food, blocks the synthesis of acetylcholine. If the messenger cannot be formed, then no messages can be carried. Paralysis sets in and death occurs, usually by respiratory failure.

Curare, atropine, and some of the local anesthetics (chapter 19) act by blocking receptor sites. When such compounds are present, the message is sent but not received. This can be good, in the case of local anesthetics, for relief from pain in a limited area. But these drugs, too, can be fatal if present in sufficient quantity.

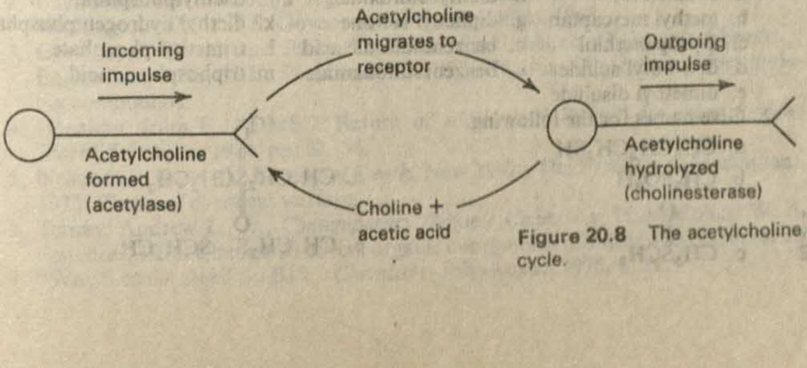

Incoming impulse
Acetylcholine migrates to receptor
Outgoing impulse
Acetylcholine formed (acetylase)
Acetylcholine hydrolyzed (cholinesterase)
Choline + acetic acid

Figure 20.8 The acetylcholine cycle.

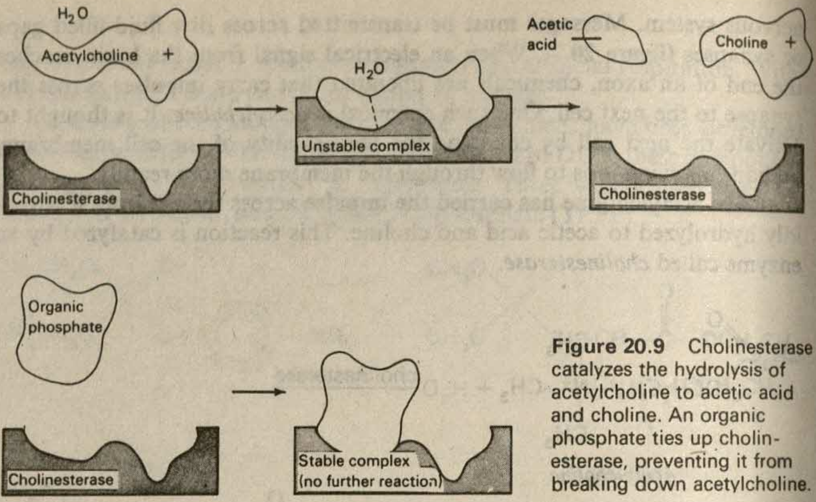
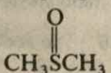
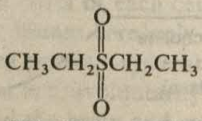


Figure 20.9 Cholinesterase catalyzes the hydrolysis of acetylcholine to acetic acid and choline. An organic phosphate ties up cholinesterase, preventing it from breaking down acetylcholine.

A third category of poisons, called anticholinesterase poisons, blocks the action of cholinesterase, the enzyme responsible for deactivating the messenger after the message is delivered. The organophosphorus compounds (section 20.10) are well-known nerve poisons. The phosphorus-oxygen linkage is thought to bond tightly to cholinesterase (**figure 20.9**), preventing the enzyme from carrying out its normal function. If the breakdown of acetylcholine is blocked, then this messenger compound builds up, causing the receptor nerves to "fire" repeatedly, to be continuously "on." This overstimulates the muscles, glands, and organs. The heart beats wildly and irregularly. The victim goes into convulsions and dies quickly.

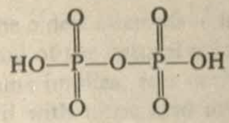
Let's not end the chapter on such a negative note, however. Certainly the nerve gases have a tremendous potential for abuse. Fortunately, none have yet been used against human populations in war. And these frightening compounds have helped us gain an understanding of the chemistry of the nervous system. It is that knowledge which enables scientists to design antidotes for the nerve poisons. Increased understanding should also contribute to our progress along more positive lines, in the control of pain, for example.

Problems

1. Write structural formulas for the following.
   a. ethanethiol
   b. methyl mercaptan
   c. 2-propanethiol
   d. di-*n*-butyl sulfide
   e. dimethyl disulfide
   f. diethyl sulfoxide
   g. diphenyl sulfone
   h. benzenesulfonic acid
   i. benzenesulfonamide
   j. triethylphosphine
   k. diethyl hydrogen phosphate
   l. trimethyl phosphate
   m. triphosphoric acid
2. Give names for the following.
   a. $CH_3CH_2CH_2SH$
   b. CH_3SO_3H
   c. 
   $CH_3\overset{\overset{O}{\|}}{S}CH_3$
   d. 
   $CH_3CH_2\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}CH_2CH_3$
   e. $CH_3CH_2S—SCH_2CH_3$

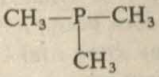
f. $CH_3CH_2SCH_3$

g.



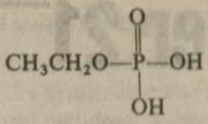
$HO{-}\overset{O}{\underset{O}{P}}{-}O{-}\overset{O}{\underset{O}{P}}{-}OH$

h.



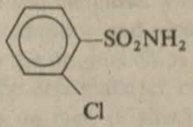
$CH_3{-}\underset{CH_3}{P}{-}CH_3$

i.



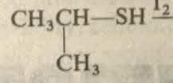
$CH_3CH_2O{-}\overset{O}{\underset{OH}{P}}{-}OH$

j.



3. Write the structural formula for the main product in each of the following reactions.

a.



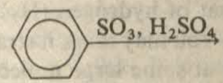
$CH_3\underset{CH_3}{C}H{-}SH \xrightarrow{I_2}$

b. $CH_3S{-}S{-}CH_3 \xrightarrow{Zn,\ H_2SO_4}$

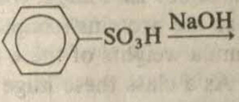
c. $CH_3CH_2SCH_2CH_3 \xrightarrow{H_2O_2,\ 25\ ^\circ C}$

d. $CH_3CH_2SCH_2CH_3 \xrightarrow{2\ H_2O_2,\ 100\ ^\circ C}$

e.



f.



g. $2\ CH_3SH \xrightarrow{Hg^{2+}}$

4. What is the structural difference between an ABS and an LAS detergent? What is the significance of this difference for the environment?
5. Describe three ways that the acetylcholine cycle can be stopped. Give examples of poisons that work each way.
6. How does BAL work as an antidote for mercury poisoning?
7. How might atropine work as an antidote for poisoning by an organic phosphorus nerve poison?

References and Readings

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chapter 21

Polymers

Chemistry is primarily a molecular science, a study of molecules. Up to now we have considered molecules as small as that of hydrogen (H_2) and as complicated as that of reserpine ($C_{33}H_{40}N_2O_9$). You may think it strange, then, when we say that we are now going to look at some large molecules. If reserpine (section 19.12) with a formula weight of 609 isn't large, what is? Well, starch and cellulose (chapter 22) are, and so are proteins (chapter 24) and nucleic acids (chapter 25). The average formula weights of these materials run into the thousands and even millions. As a class these huge compounds and others of comparable size are referred to as macromolecules (from the Greek *makros*, "large" or "long").

The naturally occurring macromolecules mentioned above are the stuff of which living things are made. They have also served humanity for centuries in the form of wood, wool, paper, cotton, and silk, as clothing and housing, and, of course, as food.

It took many years for scientists to discover that at least some of the special properties of these substances, particularly physical properties such as tensile strength and flexibility, were related to the enormous size of their constituent molecules. And it took even longer for them to determine the structure of these molecules. The major finding of these studies was that the giant molecules were constructed from "building blocks," smaller, repeating units like the bricks that make up a wall.

The temptation to improve on nature has always been very great, and it has rarely been resisted. Chemists studying the structure and properties of the macromolecules of nature soon began producing their own macromolecules, designed for specific purposes and with certain properties enhanced to suit those purposes.

We are only one chapter away from studying nature's handiwork in detail. Right now we'll spend a little time looking at the products which nature inspired.

21.1 What Happens When You Fool with Mother Nature

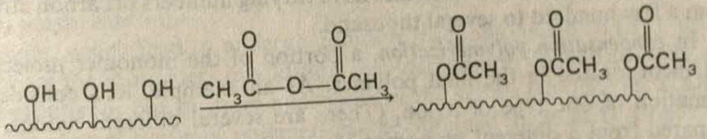
The oldest attempts to improve on nature simply involved chemical modification of the natural macromolecules. The synthetic material celluloid, as its name implies, was derived from natural cellulose. When cellulose was treated with nitric acid and then with camphor and alcohol, the product which resulted bore little resemblance to the original chips of wood or fibers of cotton (good sources of cellulose). The new material, celluloid, could be molded into hard, smooth balls. It was, in fact, originally developed as a substitute for the ivory used in billiard balls. It was also used in the film of early movies and to make stiff collars which didn't require repeated starching (accepted male apparel in the early 20th century). Because of its dangerous flammability, celluloid was eventually removed from the market.

DU PONT AMERICAN INDUSTRIES
CHALLENGE CLEANABLE COLLARS
Reduce high cost of living — save labor and starch
THE ARLINGTON WORKS
725 Broadway, New York
DU PONT

Figure 21.1 Celluloid, a nitrocellulose product, was the first synthetic plastic. Around the turn of the century, many commercial uses were found for celluloid. (Courtesy of E. I. du Pont de Nemours and Company, Inc., Wilmington, Del.)

Two other modifications of cellulose are still in use today. Cellulose can be treated with sodium hydroxide (NaOH) and carbon disulfide (CS_2) to produce a water-soluble intermediate, cellulose xanthate. A thick solution of this material is forced through fine holes into a dilute sulfuric acid solution which regenerates cellulose as fine, continuous, cylindrical threads called *rayon*. If the solution is forced through a narrow slit, a thin transparent film or sheet of the same material is obtained. In this form, however, the product is called *cellophane*. In 1927 cellophane in the form of a transparent wrapping was quickly adopted by merchants who wanted their products to be protected but visible. It is unlikely that anyone during those early years ever imagined that the same product would serve as the dialyzing membrane in artificial kidneys (section 9.11).

Cellulose acetate (also called rayon acetate or simply acetate) results when cellulose is treated with acetic anhydride. Here, at last, is a reaction we have encountered before. Cellulose, as we shall see in chapter 22, contains many hydroxyl (—OH) groups. Like any alcohol, the cellulose reacts with acetic anhydride to form an acetate ester, a reaction which we shall represent only diagramatically.



$$\text{OH OH OH} \xrightarrow{CH_3\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}CH_3} O\overset{O}{\overset{\|}{C}}CH_3 \quad O\overset{O}{\overset{\|}{C}}CH_3 \quad O\overset{O}{\overset{\|}{C}}CH_3$$

The ester is dissolved in acetone and forced through the tiny holes in a "spinneret" (**figure 21.3**). Warm air evaporates the solvent, leaving fine, lustrous threads of rayon acetate. The difference in appearance of the natural cellulose in cotton fabrics and the semisynthetic modification is striking.

It didn't take long for the chemical industry to recognize the potential of synthetics. Scientists both in and out of industry shortly began making macromolecules from scratch (or, at least, from very small molecules).

21.2 Polymers: Making Big Ones out of Little Ones

Chemists call giant molecules assembled from much smaller building blocks *polymers* (from the Greek *poly*, "many," and *meros*, "parts"). In a laboratory (and in living systems, for that matter), the preparation of poly-

Figure 21.2 These workers are packaging disposable tubing for carrying blood during the hemodialysis process. (Courtesy of Cobe Laboratories, Inc., Lakewood, Colo.)

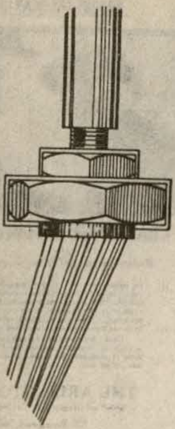
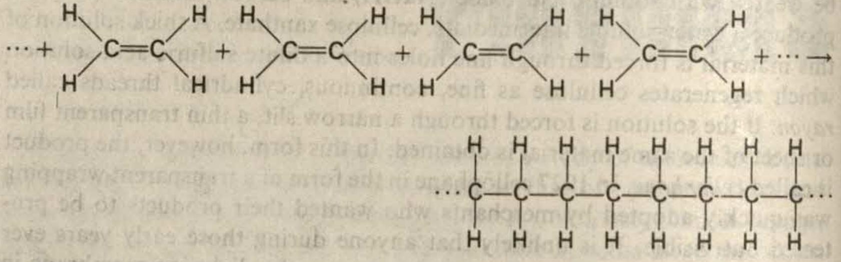


Figure 21.3 Formation of fibers by extrusion through a spinneret.

mers involves the hooking together of many smaller molecules. The small molecules, the building blocks, are called *monomers* (from the Greek *monos*, "one" and *meros*, "parts"). The polymer is as different from the monomer as long strips of spaghetti are from the particles of flour that spaghetti is made of. For example, polyethylene, the familiar solid, waxy "plastic" of plastic bags, is a polymer prepared from a monomer (ethylene) which is a gas.

There are two general types of polymerization reactions—one is called addition polymerization and the other is known as condensation polymerization.

In *addition polymerization,* the building blocks or monomers add to one another in such a way that the polymeric product contains all the atoms of the starting monomers. The polymerization of ethylene to form polyethylene can be represented by the reaction of a few monomer units.



The dotted lines in the formula of the product are like *etc.s*: they indicate that the structure is extended for many units in each direction. Notice that the two carbons and four hydrogens of each monomer molecule are incorporated into the polymer structure. Polyethylene is an addition polymer. A truer picture of the polymer is given in **figure 21.4,** which shows a framework model of a short segment. Still better is the space-filling representation of **figure 21.5.** All of these models are deficient in that they contain too few atoms. Real polyethylene molecules have varying numbers of carbon atoms—from a few hundred to several thousand.

In *condensation polymerization,* a portion of the monomer molecule is not incorporated in the final polymer. As an example, let's consider the formation of one type of nylon. (There are several different nylons, each prepared from a different monomer or set of monomers, but all share cer-

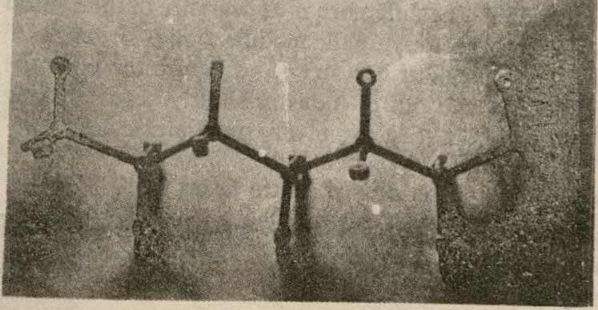


Figure 21.4 Framework model of a segment of a polyethylene molecule. (Courtesy of Science-Related Materials, Inc Janesville, Wis.)

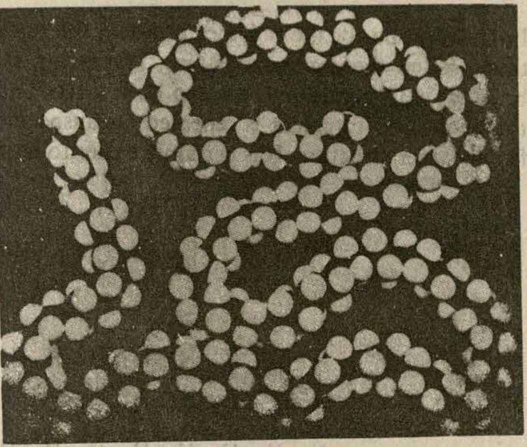
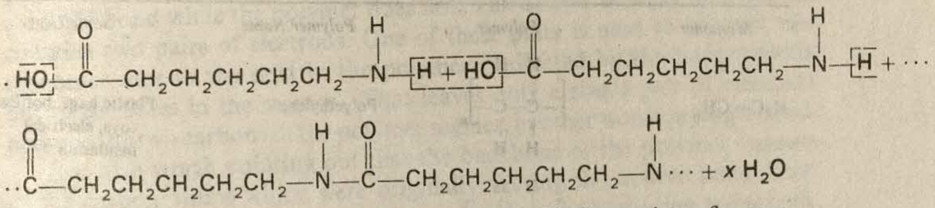


Figure 21.5 Space-filling model of a polyethylene molecule of 150 carbon atoms. (Reprinted with permission from Mandelkern, L., *An Introduction to Macromolecules*, Berlin: Springer-Verlag, 1973. Copyright © 1973 by Springer-Verlag, Inc.)

tain common structural features. We shall encounter another nylon later in this chapter.) In our present example, the monomer is 6-aminohexanoic acid. The polymerization involves the reaction of a carboxyl group of one monomer molecule with the amine group of another. This reaction produces an amide bond which holds the building blocks together in the final polymer.



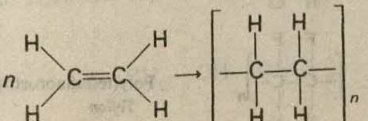
$$\cdots\boxed{\mathrm{HO}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{CH_2CH_2CH_2CH_2CH_2}-\overset{\mathrm{H}}{\overset{|}{\mathrm{N}}}-\boxed{\mathrm{H + HO}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{CH_2CH_2CH_2CH_2CH_2}-\overset{\mathrm{H}}{\overset{|}{\mathrm{N}}}-\boxed{\mathrm{H}}+\cdots$$

$$\cdots\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{CH_2CH_2CH_2CH_2CH_2}-\overset{\mathrm{H}}{\overset{|}{\mathrm{N}}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\mathrm{CH_2CH_2CH_2CH_2CH_2}-\overset{\mathrm{H}}{\overset{|}{\mathrm{N}}}\cdots+x\,\mathrm{H_2O}$$

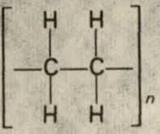
Water molecules are formed as a by-product. It is this formation of a nonpolymeric by-product which distinguishes condensation polymerization from addition polymerization.

Alkenes, which tend to undergo addition reactions (section 14.11), usually serve as the monomers in addition polymerizations. By substitution of various groups for one or more hydrogens of the simple ethylene molecule, a fantastic array of synthetic polymers can be obtained **(table 21.1)**. **Condensation polymerization** is used in the preparation of polyamides (such as nylon), polyesters (such as *Dacron*), and the polyurethanes (such as "foam rubber").

The polymerization equations we have written above are quite cumbersome. There are other ways of writing the formulas for polymers and the equations for polymerization reactions, ways which do not involve our writing out long segments of the polymer chain. We can represent the polymerization of ethylene by the equation

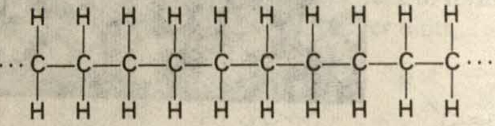


In the formula for the polymer product, the repeating polymer unit (sometimes called the *segmer,* meaning "repeating segment") is placed within brackets with bonds extending to both sides. The subscript *n* indicates that this molecular fragment is repeated an unspecified number of times in the full polymer structure. It is certainly easier to write



$$\left[-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}- \right]_n$$

than



$$\cdots-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}\cdots$$

but the latter formula is probably better at conveying the concept of a polymer as a giant molecule (even though this drawing also represents only a

Table 21.1
A selection of addition polymers

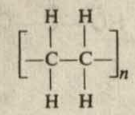
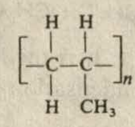
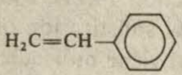
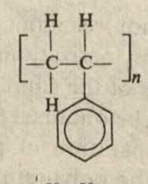
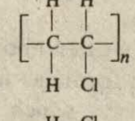
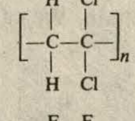
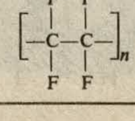
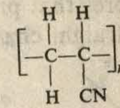
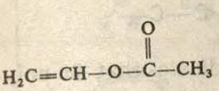
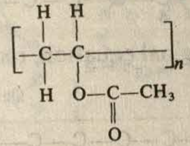
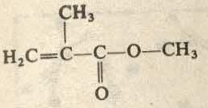
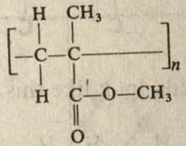
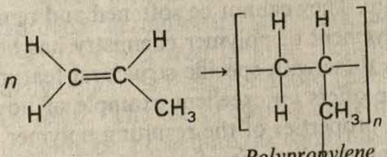
Monomer	*Polymer*	*Polymer Name*	*Some Uses*
$H_2C{=}CH_2$	 $\left[-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}- \right]_n$	Polyethylene	Plastic bags, bottles, toys, electrical insulation
$H_2C{=}CH{-}CH_3$	 $\left[-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{CH}_3}{\text{C}}}- \right]_n$	Polypropylene	Indoor-outdoor carpeting, bottles
		Polystyrene	Simulated wood furniture, styrofoam insulation and packing materials
$H_2C{=}CH{-}Cl$	 $\left[-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{Cl}}{\text{C}}}- \right]_n$	Poly(vinyl chloride), PVC	Plastic wrap, simulated leather (Naugahyde), phonograph records, garden hoses
$H_2C{=}CCl_2$	 $\left[-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{Cl}}{\underset{\text{Cl}}{\text{C}}}- \right]_n$	Poly(vinylidene chloride), *Saran*	Food wrap
$F_2C{=}CF_2$	 $\left[-\overset{\text{F}}{\underset{\text{F}}{\text{C}}}-\overset{\text{F}}{\underset{\text{F}}{\text{C}}}- \right]_n$	Poly(tetrafluoroethylene), *Teflon*	Nonstick coating for cooking utensils, electrical insulation

Table 21.1 (continued)

$H_2C{=}CH{-}CN$	 $\left[-\mathrm{CH_2}-\mathrm{CH(CN)}-\right]_n$	Poly(acrylonitrile), *Orlon, Acrilan, Creslan, Dynel*	Yarns, wigs
 $H_2C{=}CH{-}O{-}C({=}O){-}CH_3$	 $\left[-\mathrm{CH_2}-\mathrm{CH}(\mathrm{O{-}C({=}O){-}CH_3})-\right]_n$	Poly(vinyl acetate), PVA	Adhesives, textile coatings, chewing gum resin, paints
 $H_2C{=}C(CH_3){-}C({=}O){-}O{-}CH_3$	 $\left[-\mathrm{CH_2}-\mathrm{C(CH_3)}(\mathrm{C({=}O){-}O{-}CH_3})-\right]_n$	Poly(methyl methacrylate), *Lucite, Plexiglass*	Glass substitute, bowling balls

small portion of the total molecule). The simplicity of the abbreviated formula does facilitate certain comparisons between the monomer and the polymer. Notice that the monomer in the ethylene polymerization contains a double bond while the polymer does not. The double bond of the reactant contains two pairs of electrons. One of these pairs is used to connect one monomer unit to the next in the polymer (indicated by the lines sticking out to the sides in the segmer). That leaves only a single pair of electrons between the two carbons of the polymer segmer, in other words, a single bond.

It is also worth pointing out that the backbone of the polymer consists of the carbon atoms which were originally sharing the double bond. That probably sounds like a repeat of what we said in the preceding paragraph. Therefore, to make the point clearer, let's look at another polymerization reaction. This one involves propylene as the monomer.



Polypropylene

We hope that looks exactly as you expected it to look. But what if we had written the formula for propylene this way?

$$CH_2{=}CH{-}CH_3$$

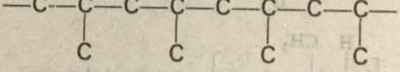
Then many novice chemists would write the abbreviated formula for the polymer this way:

$$[-CH_2-CH-CH_3-]_n$$

That formula is wrong. For one thing, it indicates that the right-hand carbon shares five bonds (a no-no). And if one ignores that problem, the formula still suggests that the polymer looks like a straight chain of carbon atoms, that is, like

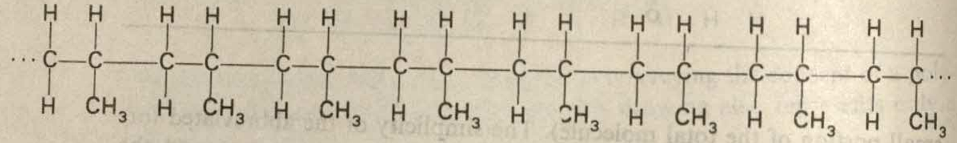
—C—C—C—C—C—C—C—C—C—C—C—C—

The correct formula, shown in the original equation, indicates that the polymer is branched.



$$—C—\underset{C}{\underset{|}{C}}—C—\underset{C}{\underset{|}{C}}—C—\underset{C}{\underset{|}{C}}—C—\underset{C}{\underset{|}{C}}—$$

Including hydrogens, the polymer would look like this.



$$\cdots\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}—\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}\cdots$$

The original doubly bonded carbons form the main chain of the polymer, and any groups attached to these carbons are attached as substituents to the main polymer chain. **Table 21.1** offers a number of examples.

21.3 The Relation of Physical Properties to Structure

Polymers are classified not only according to how they are made but also according to their reaction to heat. To the general public, synthetic polymers have come to be known as "plastics." However, *plastic* has a much more restricted meaning for chemists. The term is used to describe only those substances which can be softened by heat and then formed by pressure. In contrast, *thermosetting* polymers are those which are fusible at some stage in their production but which become permanently hard under the influence of heat and pressure. They cannot be softened and remolded.

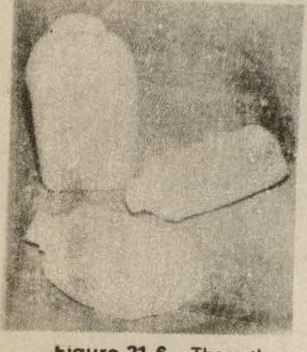


Figure 21.6 These three bottles are made of polyethylene and were heated in the same oven for the same length of time. Those which melted have branched polyethylene molecules; the other is composed of unbranched chains. (Photo by Mari Ansari.)

A major achievement of polymer chemistry has been the correlation of properties such as these with specific structural features of the giant molecules. Polyethylene offers an excellent example of how variations in structure can affect the properties of the resulting polymer. There are two kinds of polyethylene "plastics," those of high density and those of low density (**figure 21.6**). The high-density material has a greater rigidity and strength. It is used for such things as threaded bottle caps, radio and television cabinets, toys, and large-diameter pipes. Low-density polyethylenes are waxy, semirigid, translucent materials with low melting points. They are used in plastic bags, refrigerator dishes, insulation for electrical wiring, "squeeze" bottles, and many other common household articles.

What structural differences can account for these variations in properties? High-density polyethylene consists primarily of linear molecules, that is, of long, unbranched chains. These linear molecules can assume a fairly ordered crystalline structure. In such an arrangement, chains can run along-

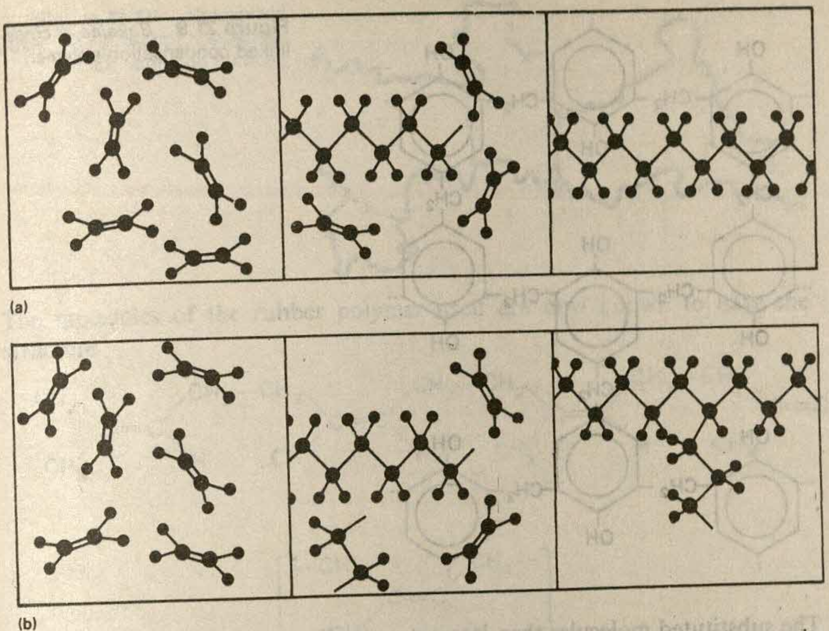


Figure 21.7 Models of an unbranched polyethylene molecule and of a chain with irregular branches. (a) Ethylene may react to form polymer molecules each of which consists of a single continuous chain, like an enormous normal alkane. Products made from unbranched polyethylene are relatively rigid. (b) Under different conditions, ethylene molecules may combine to form a polymer with side chains. These branches prevent the polymer molecules from packing together neatly. The resulting product is more flexible than the unbranched material but has a lower melting point.

side one another in close contact for relatively great distances. This permits maximum dispersion forces (section 7.4) between chains. The overall effect of increased attraction between chains is to impart strength and rigidity to the polymeric material.

The low-density polyethylenes have branched chains, which prevent the molecules from assuming a crystalline structure. The branches get in the way when two chains come into close contact (or try to). This decreases the dispersion forces and weakens the attraction between chains, resulting in the more flexible material with a lower melting point.

What if one wants a really tough material, something very strong, very rigid, something that won't melt at all on heating? The answer might be one of the oldest synthetic thermosetting polymers, *Bakelite*. *Bakelite* is a condensation polymer. It is prepared from a combination of monomers, phenol and formaldehyde, and is therefore more generally referred to as a phenol-formaldehyde resin. (The use of two or more monomers in a single polymer is not an uncommon procedure, as some later examples will indicate.) The reaction proceeds stepwise, with formaldehyde adding first to the ortho and para positions of the phenol molecule.

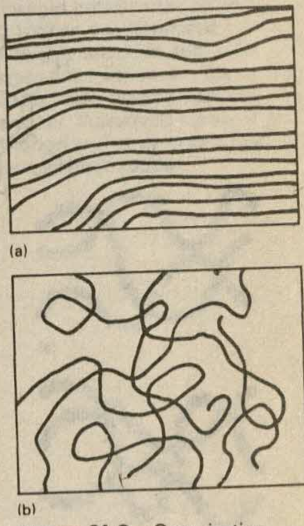
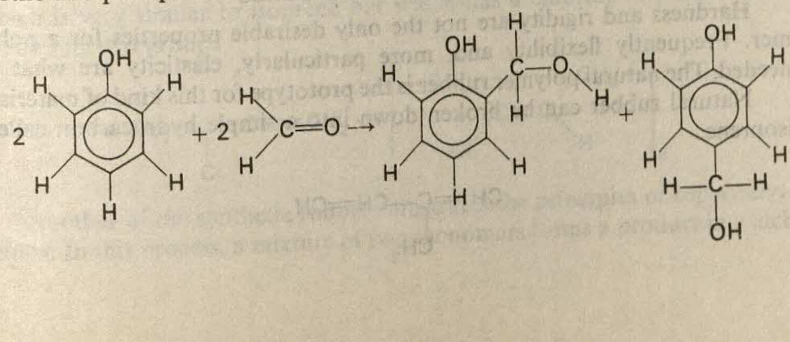


Figure 21.8 Organization of polymer molecules. (a) Crystalline arrangement. (b) Amorphous arrangement.



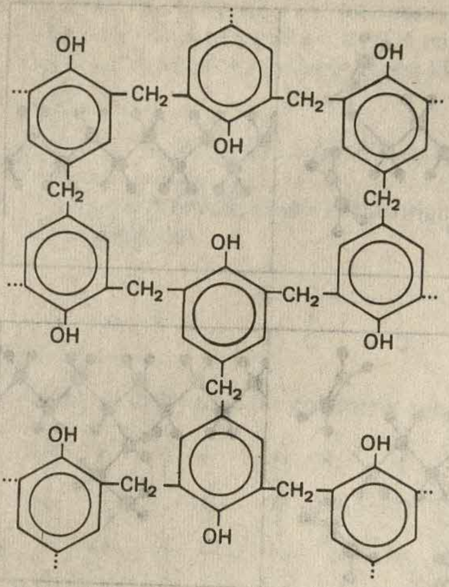
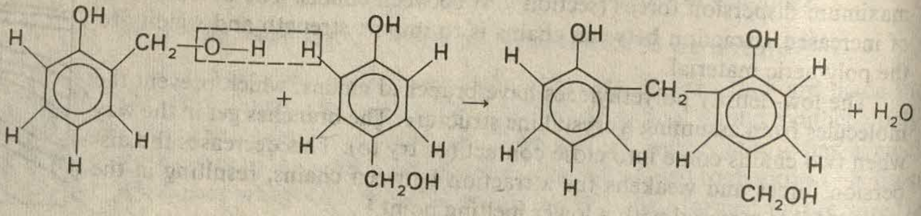


Figure 21.9 *Bakelite*, a cross-linked condensation polymer.

The substituted molecules then interact and split out water.

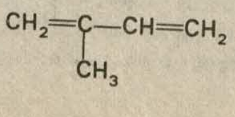


The hookup of molecules continues until an extensive network is achieved. Water is driven off by heat as the polymer sets. The final polymer is a huge, complex, three-dimensional network whose structure cannot easily be conveyed in a drawing. Nonetheless, **figure 21.9** is our attempt to do just that. The extensive cross-linking results in rigidity. The final polymer has great strength without having great weight, a most useful combination of properties.

21.4 Elastomers: More Bounce to the Ounce

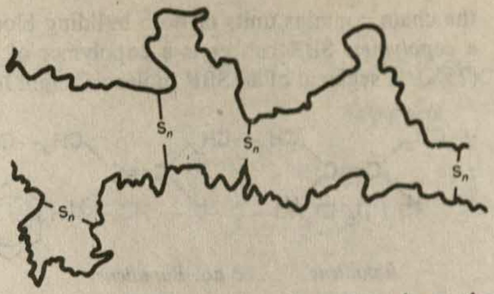
Hardness and rigidity are not the only desirable properties for a polymer. Frequently flexibility and, more particularly, elasticity are what is needed. The natural polymer rubber is the prototype for this kind of material.

Natural rubber can be broken down into a simple hydrocarbon called isoprene.

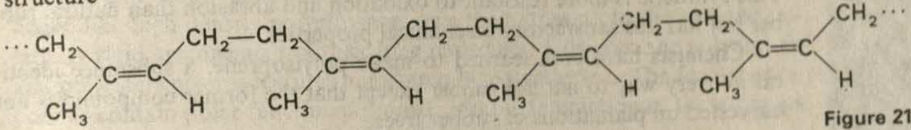


$$CH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}CH{=}CH_2$$

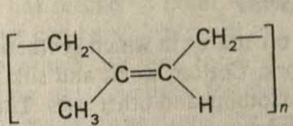
Figure 21.10 Vulcanized rubber. The subscript *n* indicates an indefinite number.



The molecules of the rubber polymer itself are now known to have the structure

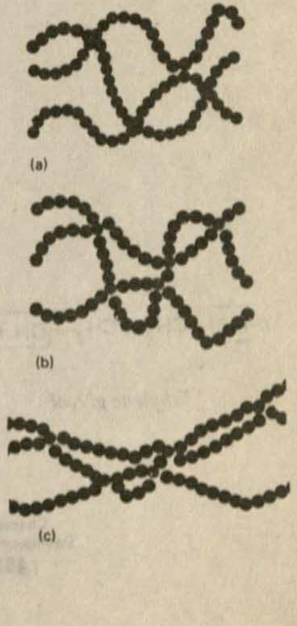


or

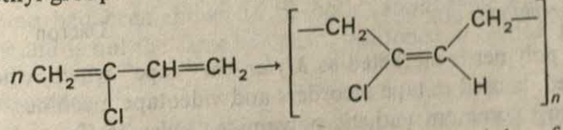


These long chains can be coiled and twisted and intertwined with one another. The stretching of rubber corresponds to the straightening of the coiled molecules. Natural rubber is soft and tacky when hot. It can be made harder by reaction with sulfur. This process, called *vulcanization,* cross-links the hydrocarbon chains with sulfur atoms (**figure 21.10**). As with the phenol-formaldehyde resin, the three-dimensional cross-linked structure makes the vulcanized rubber a harder, stronger substance, suitable for automobile tires, for example. Surprisingly, cross-linking also improves the elasticity of the rubber. With just the right degree of cross-linking, the individual chains are still relatively free to uncoil and stretch. But when a stretched piece of this material is released, the cross-links serve as a memory aid, pulling the chains back to their original prestretched arrangement (**figure 21.11**). Rubber bands owe their snap to this sort of molecular structure.

Figure 21.11 Vulcanization of rubber cross-links the molecular chains. (a) In unvulcanized rubber, the chains slip past one another when the rubber is stretched. (b) Vulcanization involves the addition of sulfur cross-linkages between the chains. (c) When the vulcanized rubber is stretched, the sulfur cross-linkages prevent the chains from slipping past one another. Vulcanized rubber is stronger and more elastic than unvulcanized rubber.

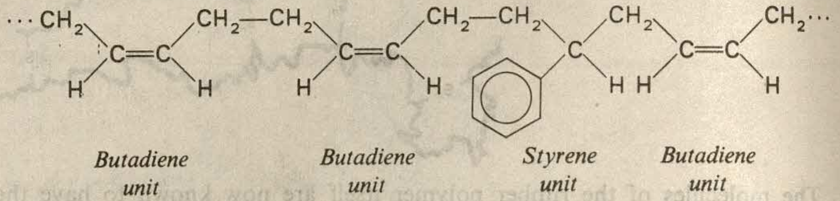


When World War II cut supplies of natural rubber, a major search for rubber substitutes was undertaken. The resulting synthetics often bear a striking molecular resemblance to nature's own elastomer. For example, the synthetic material polychloroprene (*Neoprene*) is made from a monomer which is very similar to isoprene but which has a chlorine in place of isoprene's methyl group.



$$n\,CH_2{=}\underset{\displaystyle Cl}{C}{-}CH{=}CH_2 \rightarrow \left[-CH_2-C(Cl){=}CH-CH_2- \right]_n$$

Another of the synthetic rubbers illustrates the principles of *copolymerization.* In this process, a mixture of two monomers forms a product in which the chain contains units of both building blocks. Such a material is called a *copolymer*. SBR rubber is a copolymer of styrene (25%) and butadiene (75%). A segment of an SBR molecule might look something like



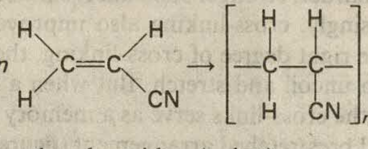
This synthetic is more resistant to oxidation and abrasion than natural rubber but has less satisfactory mechanical properties.

Chemists have even learned to make polyisoprene, a substance identical in every way to natural rubber except that the former compound is not harvested on plantations of rubber trees.

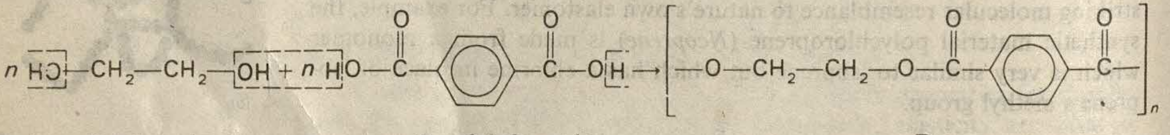
21.5 Fibers and Fabrics

Let's consider one other area in which synthetics have successfully mimicked nature's own work. Cotton, wool, and silk have long been spun and woven into fabrics for clothing and other uses. The fibrous nature and, particularly, the great tensile strength of these materials were perfectly suited to such purposes. Synthetic polymers with similar physical properties have revolutionized the clothing industry and have outdone the natural fibers in their resistance to stretching and shrinking (and to moths).

Both addition and condensation polymerization have yielded useful materials. Polyacrylonitriles (*Orlon, Acrilan, Creslan,* and the like) are addition polymers.

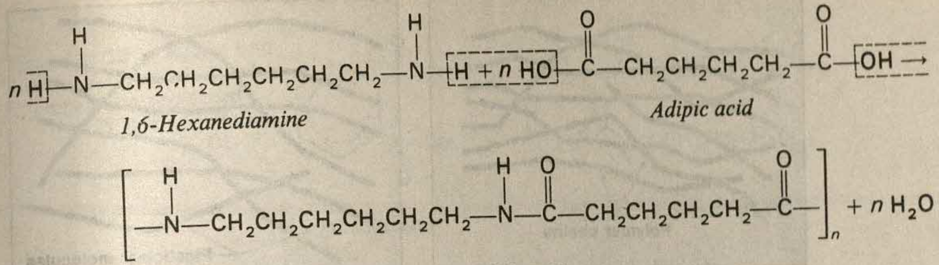


Polyesters (*Dacron*) and polyamides (nylon) are condensation polymers. *Dacron* polyester is made from the condensation of ethylene glycol with terephthalic acid.



The same polymer is marketed as *Mylar,* the "tape" which, when magnetically coated, is used in tape recorders and videotape machines.

The most common synthetic polyamide, *Nylon 66* (for a description of another nylon, see section 21.2), is also made by the condensation of two different monomers.



$$n\,\mathrm{H{-}NH{-}CH_2CH_2CH_2CH_2CH_2CH_2{-}NH{-}H} + n\,\mathrm{HO{-}\overset{O}{\overset{\|}{C}}{-}CH_2CH_2CH_2CH_2{-}\overset{O}{\overset{\|}{C}}{-}OH} \rightarrow \left[\mathrm{{-}NH{-}CH_2CH_2CH_2CH_2CH_2CH_2{-}NH{-}\overset{O}{\overset{\|}{C}}{-}CH_2CH_2CH_2CH_2{-}\overset{O}{\overset{\|}{C}}{-}}\right]_n + n\,\mathrm{H_2O}$$

Silk and wool, natural protein fibers, are also polyamides. All these fibers, like high-density polyethylene, owe their strength to the ordered, relatively rigid arrangement of their long molecules. However, the polyamides and polyesters possess features not shared by polyethylene. The former compounds contain polar functional groups, and the interaction of these groups gives these polymers their unique tensile strength.

Design of materials has reached a point where a seemingly impossible combination of properties can be incorporated into a single substance. For example, spandex fibers, which are used for stretch fabrics (*Lycra*) in ski pants, girdles, and bathing suits, combine the elasticity of rubber (necessitating coiled, flaccid molecular chains) and the tensile strength of a fiber (necessitating a crystalline arrangement of fairly rigid, highly ordered chains). How can scientists make materials such as this? By grafting two molecular structures onto one polymer chain. Blocks of components with fiber character are alternated with blocks of elastomer in the same giant molecule, and the fabric made from the polymer exhibits both sets of properties, flexibility and rigidity!

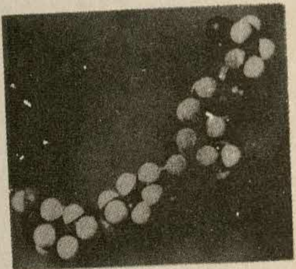
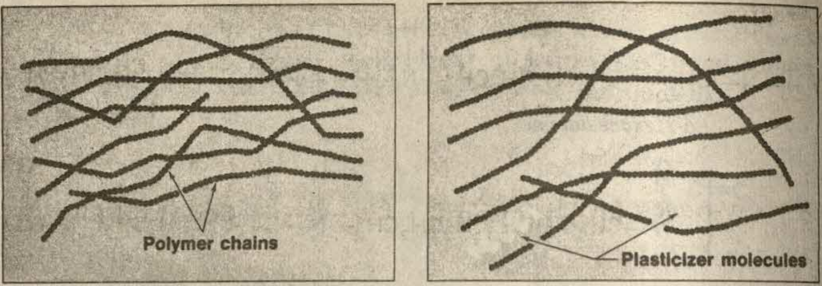


Figure 21.12 Space-filling model of a portion of *Nylon 66*. (Courtesy of E. I. du Pont de Nemours and Company, Inc., Wilmington, Del.)

The accidental ignition of fabrics, synthetic or otherwise, has caused untold human misery. The U.S. Department of Health, Education, and Welfare estimates that as many as 150 000 to 200 000 people are injured and several thousand are burned to death each year in accidents associated with flammable fabrics. While some synthetics are particularly dangerous in this regard, others may hold the answer to the problem. A good deal of research has been done to develop flame-retardant fabrics. One common approach involves the incorporation of chlorine and bromine atoms within the giant molecules of the polymeric fiber. Federal regulations require that children's sleepwear, in particular, be made of such flame-retardant materials. In 1977, the Consumer Product Safety Commission banned a flame-retardant compound called "tris" [tris(2,3-dibromopropyl)phosphate], which was used on sleepwear made from polyester and acetate fabrics. In laboratory tests, the compound had been shown to be both carcinogenic and mutagenic. (This compound is not the same as "tris" mentioned in section 19.5.)

21.6 Plasticizers

Certain polymers, particularly the vinyl types (see **table 21.1**), process with difficulty. As formed, they may be rather hard and brittle. They can be made more flexible and easier to handle by addition of chemicals called



Rigid

Less rigid

Figure 21.13 Schematic representation of how a plasticizer works. (a) Without the plasticizer, the polymer chains are rigid. (b) When plasticizer molecules are added, they slip between the larger molecules of plastic, changing the intermolecular forces and making the plastic more pliable. (Reprinted with permission from Jones, Mark M., Netterville, John T., Johnston, David O., and Wood, James L., *Chemistry, Man, and Society*, Philadelphia: W. B. Saunders, 1972. Copyright © 1972 by W. B. Saunders Company.)

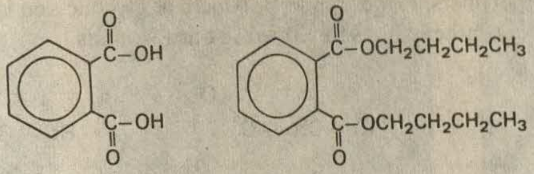
plasticizers. Ideally, these substances are liquids of low volatility. They serve as internal lubricants. Undiluted poly(vinyl chloride) (PVC) is hard and brittle. With proper plasticizers, it becomes soft and pliable. Plastic raincoats, garden hoses, and auto seat covers can be made from the modified PVC.

Plasticizers are generally lost by diffusion and evaporation as an article ages. The plastic becomes brittle, cracks, and breaks. The plasticizers in auto seat covers sometimes show up on car windows as a "fog" that is almost impossible to remove.

One type of plasticizer once used widely but now largely banned is the polychlorinated biphenyls (PCBs). These compounds were discussed in some detail in chapter 15.

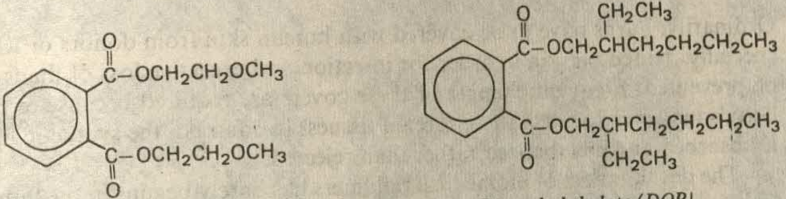
The phthalates comprise another class of plasticizers. These compounds

Figure 21.14 Some "vinyl" objects. (Photo by Dennis Tasa.)



Phthalic acid

Dibutyl phthalate (DBP)



Dimethoxyethyl phthalate (DMEP)

Dioctyl phthalate (DOP)

Figure 21.15 Phthalic acid and some derivatives. Dioctyl phthalate is also called di-2-ethylhexyl phthalate (DEHP).

are esters derived from phthalic acid. The parent acid and some of the common plasticizers derived from it are shown in **figure 21.15.** Unlike the PCBs, which are used as a complex mixture, the phthalates are generally used as separate compounds, with the individual substance chosen to impart the desired flexibility to the plastic.

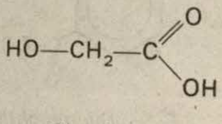
Phthalate plasticizers, like the PCBs, appear to have low acute toxicity. Their long-term effects are generally unknown. Phthalates have been leached from the PVC bags in which whole blood has been stored. It has been proposed that these plasticizers may contribute to shock lung, a sometimes fatal condition observed in some patients after a blood transfusion. Phthalates have been found in the heart muscle of cattle, dogs, rabbits, and rats. Very high dosages can induce mutations and birth defects in laboratory animals. What implication, if any, these findings have for human health is still being debated.

Figure 21.16 A plastic heart valve can be used to replace a damaged or diseased valve in the human heart. (Courtesy of General Motors Corporation, Detroit.)

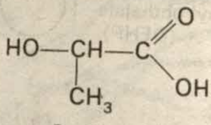
21.7 People of Plastic Parts: Biomedical Polymers

One of the most interesting uses of polymers has been in replacements for diseased, worn out, or missing parts of the human body. Artificial ball-and-socket hip joints made of steel (the ball) and plastic (the socket) are now being installed at a rate of 25 000 a year. People crippled by arthritis are not only freed from pain but are given much more freedom of movement. Patients with heart and circulatory problems can enter a hospital for a "valve job" or the replacement of worn out or damaged parts. Plastic heart valves (**figure 21.16**) are available in a variety of shapes and materials. Knitted *Dacron* tubes replace arteries blocked or damaged by atherosclerosis. Plastic implants reconstruct breasts removed because of cancer.

On contact with most foreign substances, blood begins to clot. To prevent such a reaction, most synthetics must be chemically treated and coated with heparin, a natural anticoagulant, before being used as implants. *Dacron* can be used for artificial arteries because it is relatively inert in this regard. Another approach to the problem of substituting synthetic materials for body parts is to use naturally occurring substances to construct the biomedical polymers. For example, polymers of glycolic and lactic acids have been used in synthetic films for covering burn wounds.



Glycolic acid



Lactic acid

Ordinarily, burns have to be covered with human skin from donors or with specially treated pigskin in order for infection and excessive loss of fluids to be prevented. Frequent changes of these covers are required because of the body's tendency to reject these foreign tissues. In contrast, the synthetic film is absorbed and metabolized rather than rejected.

The development of biomedical polymers has barely begun. In the future lies the prospect of the replacement of entire parts of the body. Completely artificial hearts may someday keep us alive without the need of donors for transplants and without the problem of rejection. **Figure 21.17** shows an experimental artificial heart which kept a calf alive for 48 hours.

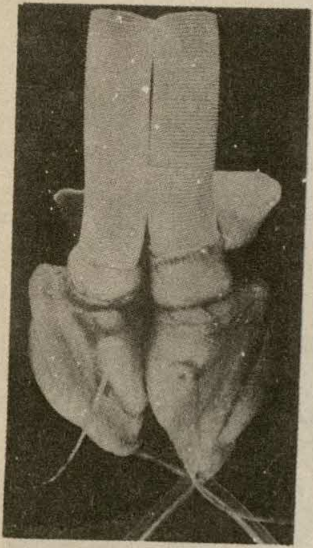


Figure 21.17 Someday soon a damaged or diseased heart may be replaced by a plastic one such as this. (Reprinted with permission from DeBakey, Michael E., et al., "Orthotopic Cardiac Prosthesis: Preliminary Experiments in Animals with Biventricular Artificial Heart," *Cardiovascular Research Center Bulletin*, April-June 1969. Copyright © 1969 by Baylor College of Medicine.)

21.8 What to Do with Them When We're Through with Them

Synthetic polymers have become an important part of our lives, largely because they do so many jobs so well. It may be that in one respect these materials are too good: they last almost forever! Once they are dumped into the environment, they tend to remain there. On land they contribute to the unsightly litter scattered along roadways and elsewhere, and they also provide breeding grounds for disease-carrying insects and rodents. Not only are "plastic" discards also found in all the oceans of the world, but they may represent a fairly immediate danger to some fish. Small fish have been found dead with their digestive tracts clogged by fragments of plastic foam the fish had ingested with their food.

Even if everyone pitches in so that, instead of being scattered all over, "plastics" are collected in refuse containers, there are still problems. Solid wastes are frequently disposed of at sanitary landfills. In our throw-away, no-deposit-no-return, use-it-once society, we are rapidly running out of dumps to accommodate the tremendous volumes of solid waste we produce. And synthetic polymers, though buried, do not rot and go away. Present research is aimed at the development of polymers that break down upon exposure to sunlight or soil microorganisms (**figure 21.18**).

Another approach to the problem is to encourage the reuse or recycling of synthetics (and everything else). Thermoplastic polymers can be melted down and remolded. Recently, methods for recycling thermosetting polymers have been developed. But both procedures require energy, something we must also begin to conserve. In addition, the discarded synthetics must first be collected and then separated from other types of solid waste and from each other.

There is another way to dispose of discarded "plastics," and that is to burn them. But this can lead to an increase in air pollution. Automobile

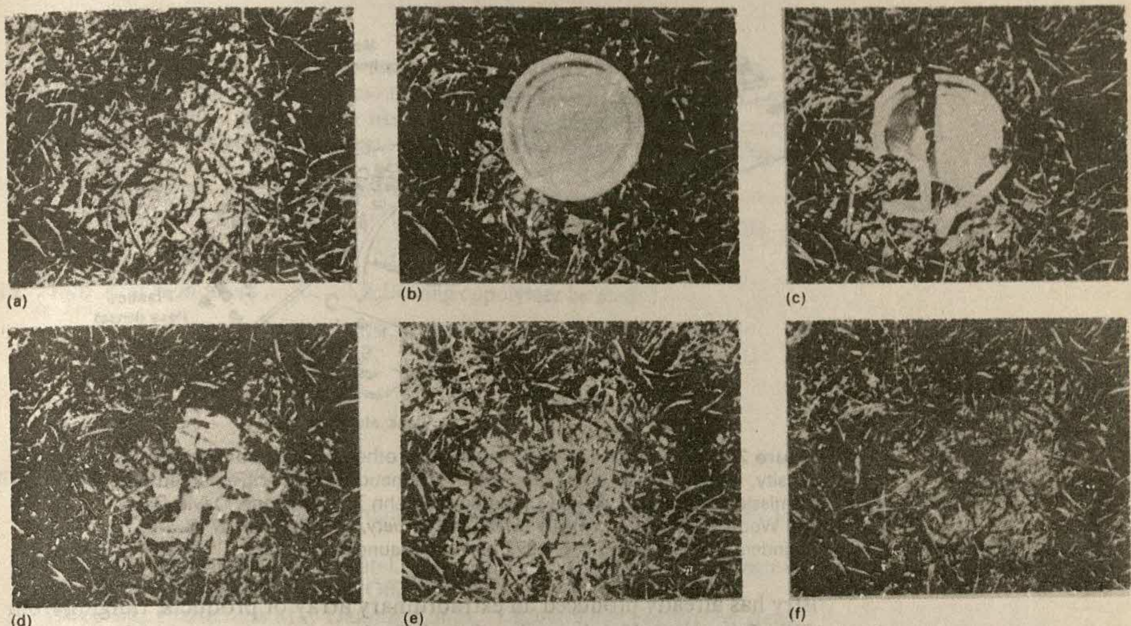


Figure 21.18 This sequence of photos shows the average rate of decomposition of a standard plastic cup lid made with new biodegradable plastic. The decomposition process is a controllable and predictable photochemical reaction. (a) At 0 days, the environment is clean and free of litter. (b) At 5 days, a cup lid made with biodegradable plastic additive is introduced into the environment. (c) After 30 to 90 days, the lid begins to break apart, signaling that decomposition is well under way. (d) After 60 to 120 days, the lid is totally fragmented. (e) After 90 to 150 days, only a fine powder remains. (f) After 6 to 12 months, the environment is once again free of litter. No evidence of the cup lid remains. (Courtesy of Bio-Degradable Plastics, Inc., Sioux Falls, S. Dak.)

tires burn with a sooty, stinking smoke, and poly(vinyl chloride) produces toxic hydrogen chloride gas when it burns. Incinerators are corroded by acidic gases and clogged by those plastics which melt from the heat without burning.

Problems associated with the burning of synthetics are not limited to disposal procedures. Toxic gases are produced when many of these polymers are accidentally ignited. In December 1972 lethal amounts of cyanide were found in the bodies of victims of a plane crash in Chicago. The Illinois Department of Law Enforcement traced the cyanide to burning synthetics in the plane's cabin. Tests at the University of Wisconsin at River Falls showed that hydrogen cyanide is formed in large quantities by the burning of polyacrylonitriles (such as *Orlon, Creslan,* and *Acrilan*) and other nitrogen-containing polymers. The increasing use of synthetic polymers in home furnishings and construction calls for more research to identify—and quantify—products from the combustion of these materials.

Certainly, the dangers associated with synthetic polymers are not the only justification for further research. This relatively young branch of chem-

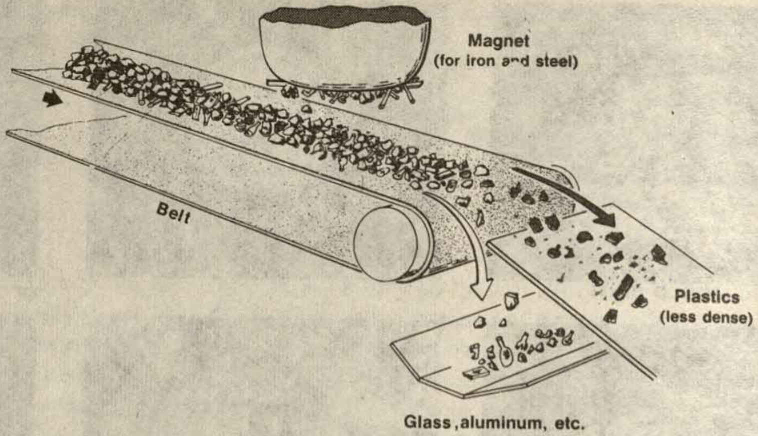
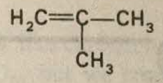


Figure 21.19 Plastics can be separated from other wastes by differences in density. Iron and steel can be removed by magnetic attraction. (Reprinted with permission from Jones, Mark M., Netterville, John T., Johnstone, David O., and Wood, James L., *Chemistry, Man, and Society,* Philadelphia: W. B. Saunders, 1972. Copyright © 1972 by W. B. Saunders Company.)

istry has already produced an extraordinary array of products, ranging from *Silly Putty* to artificial arteries. It is difficult even to guess what future polymers might be able to do, but it is almost a certainty that many of them will be devised to answer critical needs of our society.

Problems

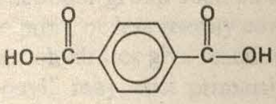
1. Define these terms.
   a. macromolecule
   b. polymer
   c. monomer
   d. segmer
   e. addition polymerization
   f. condensation polymerization
   g. vulcanization
   h. elastomer
   i. copolymer
   j. plasticizer
2. Make a list of "plastic" objects in your room. Try to identify a few of the kinds of polymers used in making these items.
3. What do celluloid, cellophane, rayon, and rayon acetate have in common?
4. How do thermosetting and thermoplastic polymers differ in terms of structure and properties?
5. What structural feature is usually found in molecules used as monomers for addition polymerization?
6. Why is rubber elastic? How does vulcanization improve its elasticity?
7. How do low-density and high-density polyethylene differ in terms of structure and properties?
8. What problems arise when "plastics" are disposed of in landfills? By incineration?
9. Should "plastics" be
   a. totally banned?
   b. selectively banned?
   c. used without regulation?
   d. used with some regulation?
10. Where will "plastics" come from when the earth's supply of coal and petroleum is exhausted?
11. Isobutylene polymerizes to form a product called butyl rubber. Write a two-dimensional representation of a segment of the butyl rubber molecule. The segment should contain at least four monomer units. The structure of isobutylene is

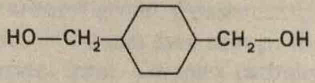


$$H_2C{=}\underset{\displaystyle CH_3}{C}{-}CH_3$$

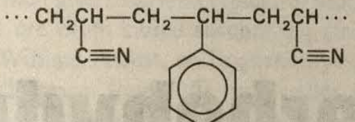
Draw the segmer and the abbreviated formula for this polymer.

12. *Kodel* is a polyester fiber. The monomers are terephthalic acid and 1,4-cyclohexanedimethanol, or 1,4-bis(hydroxymethyl)cyclohexane. Write the structure of *Kodel* using the abbreviated segmer formula. Structures of the monomers are





13. From what monomers might the following copolymer be made?



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chapter 22

Carbohydrates

Almost everyone knows what carbohydrates are: they're what you eat or don't eat depending on whose diet book you fancy. In fact, as any dietician or nutritionist will tell you, carbohydrates must be included in any well-balanced diet. They are the body's primary source of energy. This energy is stored in the complex molecular structure of the carbohydrates when these compounds are synthesized by green plants from carbon dioxide and water. The entire biosphere, and that includes us, is dependent on the endothermic reaction in which simple compounds plus energy yield complex compounds. When we metabolize the complex compounds, the atoms rearrange themselves back into simple compounds and, in the process, release their stored energy for our use.

The photosynthetic reaction in green plants produces glucose. This simple sugar can be used by the plant for energy, or it can be converted to a more complex form—starch—to serve as a source of energy for later use, perhaps as nourishment for the plant's seeds. Some of the glucose is converted to cellulose, the structural material of plants. We can gather and eat the parts of plants that store energy—seeds, roots, tubers, fruits—and use some of that energy for ourselves. We can eat the cellulose, too, but we can't get any energy from it. Why? The answer lies in the chemical structure of cellulose.

We'll discuss the metabolism of carbohydrates in chapter 30. For now, let's look at their structures and some simple reactions.

22.1 Carbohydrates: Definitions and Classifications

Carbohydrates are compounds of carbon, hydrogen, and oxygen. They include the starches, the sweet-tasting compounds called sugars, and the structural materials such as cellulose. The term *carbohydrate* has its origins in the fact that the molecular formulas of many of these substances can be rearranged so that they look like carbon hydrates. For example, the formula for blood sugar is $C_6H_{12}O_6$, but we could also represent it as $(C \cdot H_2O)_6$. These compounds are not hydrates of carbon, however. They are alcohols, all containing the hydroxyl (—OH) functional group. Most contain a real or latent carbonyl (C=O) group. By a *latent* carbonyl group we mean a functional group such as a hemiacetal or an acetal (chapter 17) which can be more or less readily converted to a carbonyl group. Consequently, some carbohydrates give reactions as aldehydes or ketones even though the "carbonyl" may exist primarily in a hemiacetal form. Complex carbohydrates containing the acetal function can be hydrolyzed like other acetals to simpler compounds which give reactions typical of aldehydes or ketones.

Carbohydrates are often called saccharides (from the Latin *saccharon,* "sugar"). In fact, William Proust, an English physician who first recognized the three general classes of foodstuffs (now called carbohydrates, fats, and proteins), suggested that they be called the saccharine, the oily, and the albuminous. Simple carbohydrates, those which cannot be further hydrolyzed, are called monosaccharides. Carbohydrates which can be hydrolyzed to two monosaccharide units are called disaccharides, and carbohydrates which can be hydrolyzed to many monosaccharide units are called polysaccharides.

Sugars are also classified experimentally into two groups. Those which reduce Tollens' reagent (or related reagents) are called *reducing sugars* (section 22.6). Those which give a negative test, that is, which are not readily oxidized, are called *nonreducing sugars.*

22.2 Monosaccharides: Further Classifications

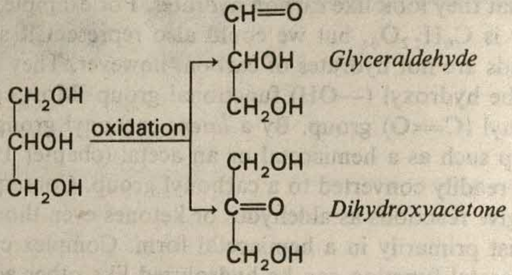
Monosaccharides are further classified by the number of carbon atoms per molecule.

Number of Carbon Atoms	*Class*
3	Triose
4	Tetrose
5	Pentose
6	Hexose
7	Heptose

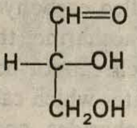
The *-ose* ending indicates a carbohydrate; the prefixes we have encountered previously.

Still another system classifies monosaccharides on the basis of the carbonyl group present. Those that have an aldehyde group are called aldoses, and those with a ketone group are called ketoses. The two systems are often combined. For example, an aldopentose is a monosaccharide with five carbon atoms and an aldehyde function. Similarly, a ketohexose has six carbons and a ketone function.

The simplest sugars are the trioses. Two of these are derived from glycerol by oxidation. These trioses are important intermediates in the metabolism in muscles. Dihydroxyacetone is a ketotriose. Glyceraldehyde is an aldotriose.



It should be noted that glyceraldehyde, like amphetamine (chapter 19), exhibits "handedness." It exists in two nonidentical mirror image forms.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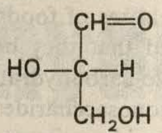
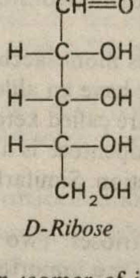

II

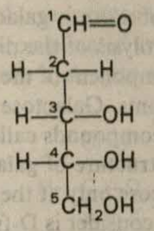
Formula I, with the aldehyde group ($CH{=}O$) at the top and the primary alcohol group (CH_2OH) at the bottom, has the hydrogen on the left and the hydroxyl on the right. Chemists refer to arrangement I as the D configuration. Arrangement II is said to have the L configuration.

All the important carbohydrates are related to D-glyceraldehyde. They have the same "handedness" about the carbon atom just above the primary alcohol group. All these sugars are said to be members of the D series. Such handedness is of considerable importance. We cannot obtain energy from L carbohydrates (though beings on some other planet, with enzymes that are mirror images of ours, might be able to use only L forms). Since we will encounter only D carbohydrates, we will not emphasize this form of isomerism here. The interested reader is urged to see the references cited at the end of this chapter, particularly reference 2.

There are two aldopentoses of interest to us. One is D-ribose, the sugar unit which occurs in ribonucleic acids (RNA).


D-Ribose

Related to D-ribose, but not an isomer of it (its molecular formula is different), is D-2-deoxyribose, the sugar unit which occurs in deoxyribonucleic acids (DNA).



D-2-Deoxyribose

As the prefix *deoxy-* implies, this sugar is "missing" an oxygen on the second carbon atom. We will encounter these compounds again in chapter 25. For now, though, let's look at some hexoses. There are 16 isomeric aldohexoses, but we shall discuss only 3 of them here. There are quite a few ketohexoses, too, but we shall deal with only a single ketohexose here. All of the sugars we discuss in the remainder of this chapter belong to the D family. If no family designation is given, you can assume the compound is a D sugar.

22.3 D-Glucose: Sugar, Sugar, Everywhere

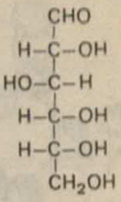
D-Glucose is undoubtedly the most important hexose. This sugar is sometimes called dextrose. D-Glucose is the normal "blood sugar," making up about 0.065% to 0.110% (a concentration of 65 to 110 mg %) of our blood. It is essential to life, for it is the only sugar our cells can use directly for the production of energy. Other sugars must be converted to glucose before we can use them.

Glucose is readily available from the hydrolysis of starch and cellulose (sections 22.8 and 22.9). It occurs, along with sucrose (section 22.7) and fructose (section 22.4), in the sap of plants. Honey is mainly a mixture of glucose and fructose. It has been estimated that half of the carbon atoms in the biosphere are tied up in glucose. Unfortunately for the hungry people of the world, most of it is in the form of cellulose, which has little or no food value for humans.

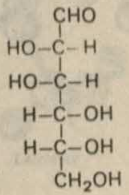
Figure 22.1 illustrates D-glucose. This formula follows our convention of writing the aldehyde group at the top and the primary alcohol group at the bottom. Glucose is a D sugar because the hydroxyl group at the fifth carbon (the one just above the CH_2OH) is on the right. In fact all the hydroxyl groups except that at the third carbon are to the right. You should learn to draw this formula for glucose, as well as the analogous formulas for the other three monosaccharides in **figure 22.1.**

22.4 Mannose, Galactose, and Fructose

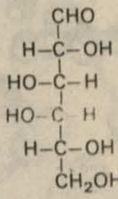
Of the remaining aldohexoses, only two occur widely in nature. Mannose is a component of the polysaccharide mannan, found in some berries. A particularly good source is "vegetable ivory," the endosperm of palm nuts. Buttons were once widely made from this material, with the waste being hydrolyzed to mannose. A structure for mannose is presented in **figure 22.1.** Note that the configuration differs from that of glucose only at the second carbon atom.



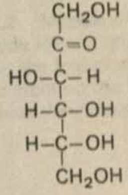
Glucose



Mannose



Galactose



Fructose

Figure 22.1 Structures of four important hexoses.

The other common aldohexose is galactose. This sugar, along with glucose, is obtained upon hydrolysis of the disaccharide lactose, or milk sugar (section 22.7). It is also a component of the polysaccharides called galactans, found in the cell walls of plants. Galactose is found in the brain and nerves, where it is a constituent of compounds called cerebrosides and gangliosides. **Figure 22.1** also shows the structure of galactose. Notice that the configuration differs from that of glucose only at the fourth carbon atom.

The only ketose we shall consider is D-fructose, whose structure is shown in **figure 22.1.** It occurs, along with glucose and sucrose, in honey and fruit juices. It is the only sugar found in the semen of bulls and men. Fructose and glucose are obtained by the hydrolysis of the disaccharide sucrose, or table sugar (section 22.7). Fructose is also called levulose.

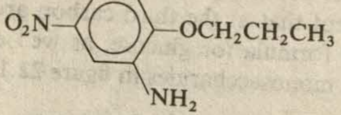
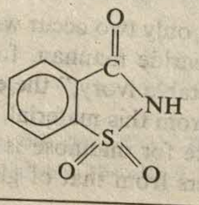
Fructose is the sweetest of the common sugars (**table 22.1**). Many nonsugars are several hundred or several thousand times as sweet, however.

Structurally, fructose is a 2-ketohexose. From the third through the sixth carbon atoms its structure is the same as that of glucose.

22.5 More on Monosaccharides

So far we have represented the monosaccharides as hydroxyaldehydes and ketones. These representations account for many of the properties (section 22.6) of these simple sugars. However, we learned in chapter 17 that aldehydes and ketones react with alcohols to form hemiacetals and hemiketals. You should not be surprised, then, to find that hydroxyl groups and carbonyl groups conveniently located on the same molecule react with one

Table 22.1
Sweetness of some compounds relative to sucrose as 100

Compound	*Class*	*Relative Sweetness*
Glucose	Monosaccharide	74
Fructose	Monosaccharide	173
Galactose	Monosaccharide	70
Lactose	Disaccharide	16
Sucrose	Disaccharide	100
Maltose	Disaccharide	33
P-4000		400 000
Saccharin*		300

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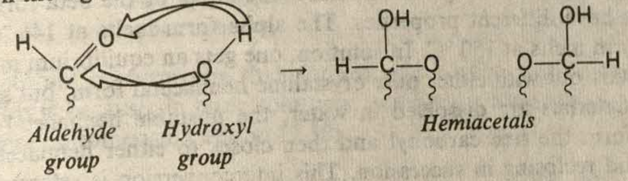
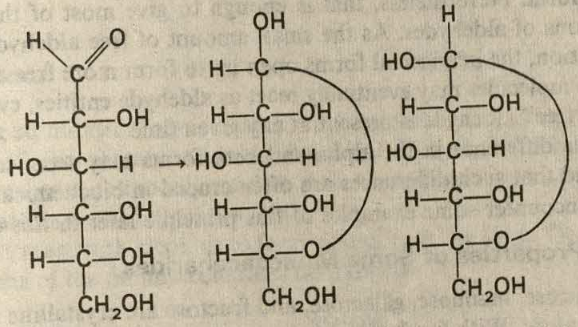
*Note that saccharin is *not* a saccharide.

another and that, consequently, the monosaccharides exist mainly as hemiacetals. The situation is further complicated by the fact that the ring can close in either of two ways, with the hydrogen on the left or with the hydrogen on the right.

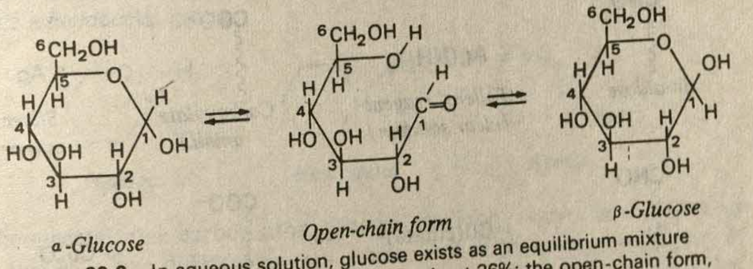


Thus, each hemiacetal exists in two forms.

Let's look at this reaction for glucose.

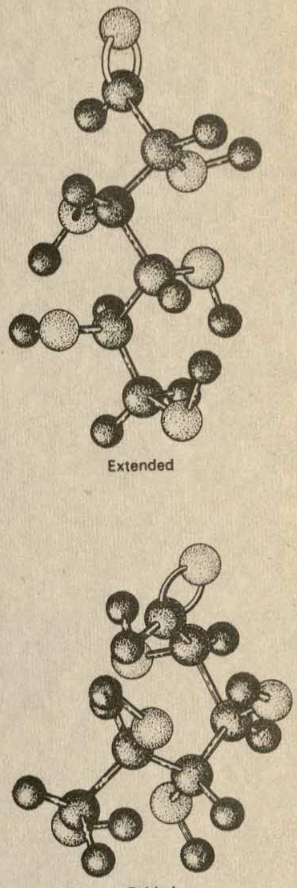


"Now wait a minute," you say. "Things are bad enough with all these complications, and now you ignore a hydroxyl group located right next to the carbonyl in order to play around with the hydroxyl at the fifth carbon. And you had to write a long, silly-looking bond to do it!" A reasonable objection—which is why we must introduce a different type of formula. In this new formula, we'll take into account approximately correct bond angles. **Figure 22.2** shows a model of the free aldehyde form of glucose. Notice how it folds around on itself. The center structure in **figure 22.3** is drawn to resemble the model. Note that the hydroxyl on the fifth carbon is quite near the carbonyl carbon, so it's not surprising that it is this hydroxyl group which reacts with the carbonyl. When the reaction occurs, the originally doubly bonded oxygen may be pushed up or down, giving rise to two different hemiacetal forms. The structure on the left, with the hydroxyl on the first



α-Glucose *Open-chain form* *β-Glucose*

Figure 22.3 In aqueous solution, glucose exists as an equilibrium mixture of these three forms. α-Glucose accounts for about 36%; the open-chain form, for about 0.02%; and β-glucose, for about 64%.



Extended

Folded

Figure 22.2 Models of the free-aldehyde form of glucose. Note that in the folded model the oxygen atom on the fifth carbon is near the carbonyl carbon.

carbon projected downward, represents what is called the alpha (α) form. That on the right, with the hydroxyl on the first carbon pointed upward, is the beta (β) form.

Crystalline glucose may exist in either the alpha or the beta form. The two forms have different properties. The alpha form melts at 146 °C, and the beta form melts at 150 °C. In solution, one gets an equilibrium mixture. You can start out with either pure crystalline hemiacetal form, but as soon as these materials are dissolved in water, the unstable hemiacetal group opens to form the free carbonyl and then closes to either hemiacetal, reopening and reclosing in succession. This interconversion is referred to as mutarotation (from the Latin *mutare,* "to change"). At equilibrium, the mixture is about 36% alpha and 64% beta. There is less than 0.02% of the aldehyde form. Nevertheless, that is enough to give most of the characteristic reactions of aldehydes. As the small amount of free aldehyde is used up in a reaction, the hemiacetal forms open up to form more free aldehyde. Thus, *all* the molecules may eventually react as aldehyde entities, even though very little "free" aldehyde is present at any given time.

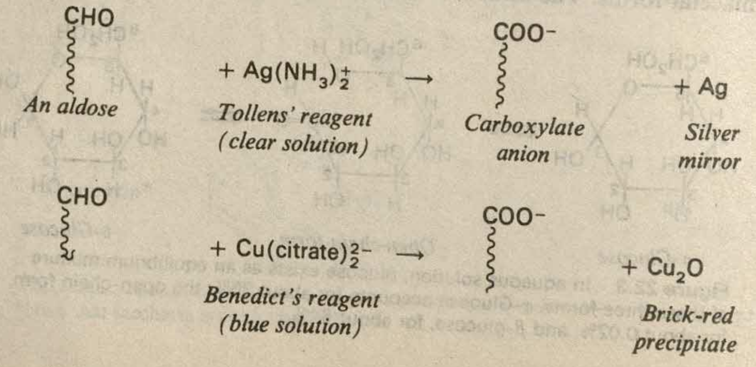
The difference in the alpha and beta forms may seem trivial, but keep in mind that such differences are often crucial in biochemical reactions. We shall encounter some examples of this principle later in this chapter.

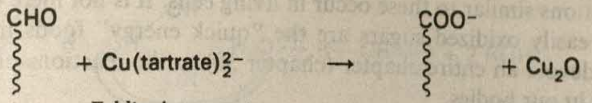
22.6 Properties of Some Monosaccharides

Glucose, mannose, galactose, and fructose are crystalline solids at room temperature. With five hydroxyl groups per molecule, these sugars are quite soluble in water.

Chemically, these monosaccharides undergo the reactions to be expected from the functional groups present. The hydroxyl groups react to form esters and ethers. These reactions, though, are more important commercially for the polysaccharide cellulose (section 22.9) than for the simpler sugars.

One important reaction is the oxidation of the aldehyde group, which is one of the most easily oxidized organic functional groups. This can be accomplished by any mild oxidizing agent. Ones frequently used are Tollens', Benedict's, and Fehling's reagents. The Tollens test is based on the reduction of silver ions, and both Benedict's and Fehling's tests involve the reduction of copper complexes. These reactions aid in the detection of reducing sugars (in the urine of diabetics, for example).

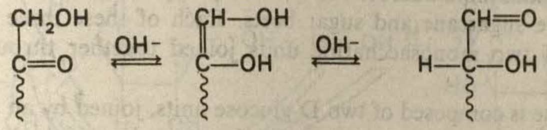




Fehling's reagent (blue solution)

Brick-red precipitate

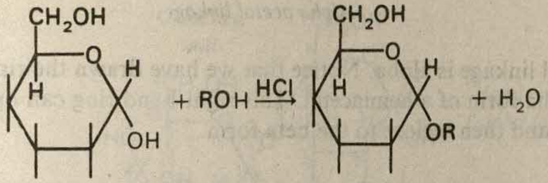
It should not be surprising that aldoses give positive tests, but ketoses do too. This is because, in basic solutions, ketoses (and aldoses) are subject to keto-enol tautomerism (section 17.10).



A ketose *An enol* *An aldose*

In the resulting equilibrium, some aldose is always formed. Because of this, basic solutions of all monosaccharides exhibit some aldehyde character. Since the oxidizing reagents commonly used to detect reducing sugars are basic, *all* monosaccharides act as reducing sugars.

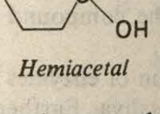
Hemiacetals react with alcohols to form acetals (section 17.8). The cyclic hemiacetal forms of the monosaccharides do likewise.



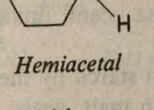
An α-aldohexose

An α-glycoside (an acetal)

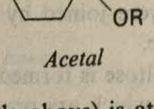
The alcohol with which the hemiacetal reacts may be as simple as methanol or as complicated as another sugar molecule (section 22.7). While hemiacetals are unstable and open up to form free aldehyde groups, the glycosides (acetals) are quite stable. They do not undergo mutarotation and do not reduce Tollens', Benedict's, or Fehling's reagents. To recognize a reducing sugar, look for a *hemi*acetal group.



Hemiacetal



Hemiacetal



Acetal

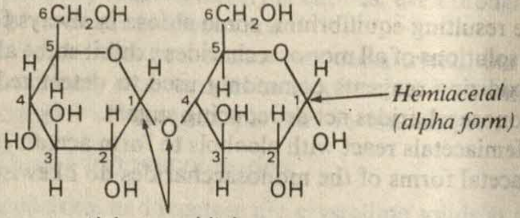
In a hemiacetal, one carbon atom (shown explicitly above) is attached by single bonds to two different oxygen atoms. One of these oxygens is part of an ether group and the other is in a hydroxyl group. Acetals, on the other hand, are 1,1-diethers.

Reactions similar to these occur in living cells. It is not mere coincidence that the easily oxidized sugars are the "quick energy" foods in our diets. We will devote an entire chapter (chapter 30) to the reactions of the carbohydrates in our bodies.

22.7 Malt, Milk, and Sugarcane: Some Disaccharides

There are three disaccharides worthy of our attention—maltose, lactose, and sucrose. Maltose occurs free, to a limited extent, in sprouting grain. Its major source, however, is the partial hydrolysis of starch. Lactose occurs in mammalian milk. Sucrose occurs widely in plant juices, but our principal sources are sugarcane and sugar beets. Each of these three disaccharides consists of two monosaccharide units joined together through an acetal linkage.

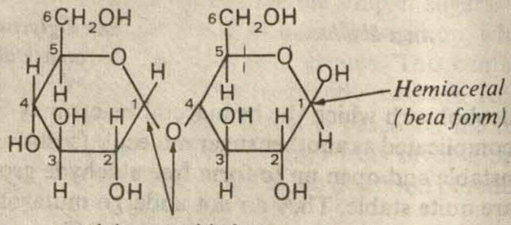
Maltose is composed of two D-glucose units, joined by an acetal linkage from the first carbon of one ring to the fourth carbon of the other.



Hemiacetal (alpha form)

Alpha acetal linkage

The acetal linkage is alpha. Notice that we have drawn the ring on the right in the alpha form of a hemiacetal. This right-hand ring can open to the free aldehyde and then reclose to the beta form.

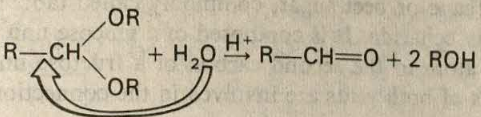


Hemiacetal (beta form)

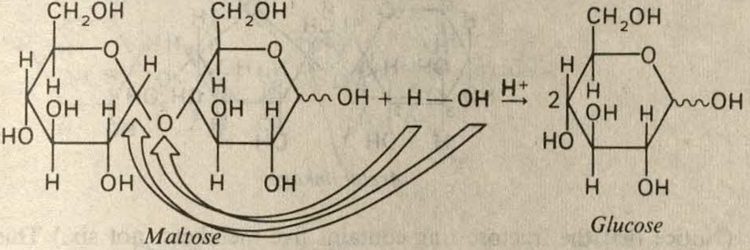
Alpha acetal linkage

Thus, maltose is a reducing sugar. It can exist in two forms, differing in configuration only about the first carbon of the right-hand ring. The acetal link *between* the two rings is fixed, however. It must remain alpha. If two glucose units were joined by a beta acetal linkage, the compound would not be maltose.

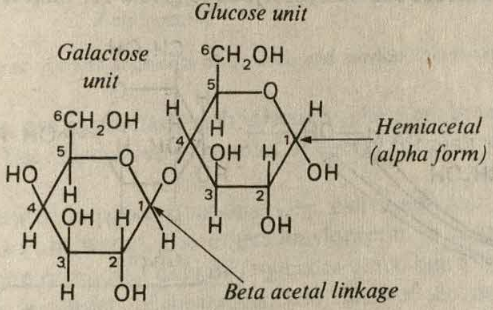
Maltose is formed from starch by the action of enzymes known as *amylases,* which are present in malt, yeast, and saliva. Further hydrolysis of maltose by the enzyme *maltase* or by dilute acid opens the acetal link between the two rings and gives glucose as the sole product. Recall that simple acetals are hydrolyzed by aqueous acid.

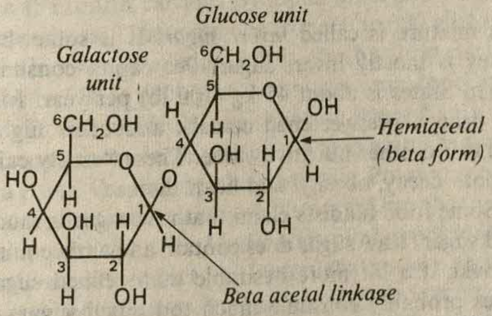


In a similar manner, the acetal linkage in maltose is hydrolyzed.



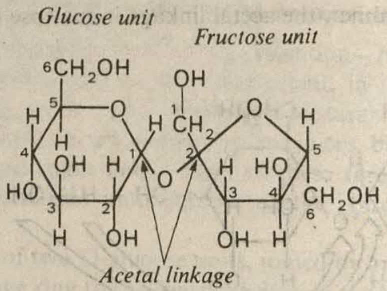
Lactose or milk sugar occurs to the extent of 5% to 7% in human milk and 4% to 6% in the milk of cattle. In lactose, a galactose unit is joined to a glucose unit. The first carbon of the galactose ring is joined by a beta acetal link to the fourth carbon of the glucose ring.





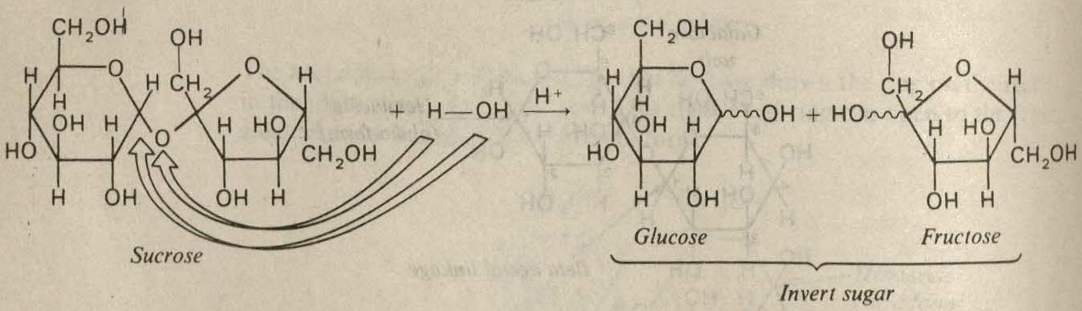
Note that lactose is also a reducing sugar because the first carbon of the glucose unit is in the hemiacetal form. Like maltose and the monosaccharides, lactose exists in two forms, alpha and beta. Lactose is hydrolyzed to one glucose unit and one galactose unit.

Sucrose (cane or beet sugar, commonly called table sugar) is the most important disaccharide. It is composed of a glucose unit joined through its first carbon atom to the second carbon of a fructose unit. The latent carbonyl groups of both units are involved in the connection between the two rings.



(Notice that the fructose ring contains five members, not six.) This is the only isomer of sucrose. Search as you may, you'll find no hemiacetal unit in sucrose. The first carbon of the glucose ring is an acetal carbon frozen in the alpha arrangement; the second carbon of the fructose ring is a ketal carbon, fixed in the arrangement shown. We have now encountered our first nonreducing sugar. Neither ring of sucrose can undergo ring opening.

Sucrose can be hydrolyzed to give a 1:1 mixture of fructose and glucose.

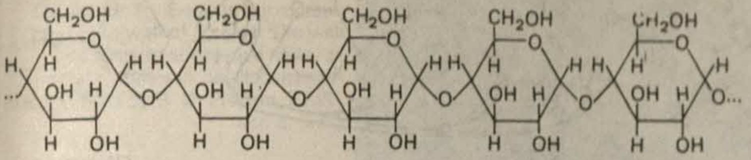


This mixture is called *invert sugar*. It is somewhat sweeter than sucrose. Honey is mostly invert sugar. Per capita consumption of sucrose in the United States is about 45 kg (100 lb) per year. Much of it is consumed in soft drinks, presweetened cereals, and other highly processed foods with little or no other nutritive value. These "empty calories" contribute greatly to tooth decay, obesity, and heart disease.

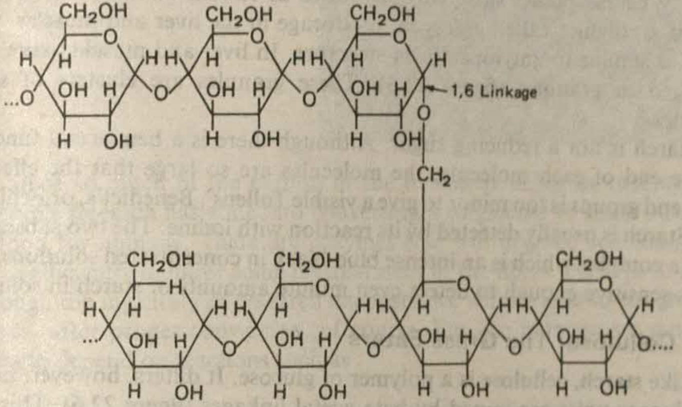
Some food faddists claim that raw sugar is much better for you than refined sugar. Raw sugar does contain a few trace minerals, but hardly enough to make it a lot more desirable than refined sugar. People in the United States probably consume much too much sugar—whether raw or refined.

22.8 Starch: The Carbohydrate Reserves

Plants make glucose by photosynthesis. They store it in the form of starch, a polymer of glucose. Plant seeds, especially the cereal grains, and



Amylose



Amylopectin

Figure 22.4 Structures of small segments of amylose and amylopectin molecules.

tubers, such as potatoes, are particularly rich in starch. These are the energy reserves for the plant. They also serve as sources of energy for animals and people who eat them.

Starch can be separated into two fractions. One, called amylose, forms a colloidal dispersion in hot water. The other, amylopectin, is completely insoluble. Both forms are composed only of D-glucose units, but they differ in several ways. Amylose consists of an unbranched chain of glucose units joined from the first to the fourth carbons by alpha linkages (the same arrangement one finds in maltose). There may be from 60 to 300 glucose units per chain. Amylopectin has similar chains, but it also has branches off the sixth carbon. There may be 300 to 6000 glucose units per amylopectin molecule. Partial structures of these molecules are shown in **figure 22.4.**

Starch in plants occurs as very large granules. These granules rupture in boiling water to form a paste. On cooling, the paste gels. Potatoes and cereal grains, when cooked in water, form this type of "starchy" broth.

Commercial starch is a white powder. Under controlled conditions, starch can be partially hydrolyzed to products of intermediate molecular weight called *dextrins.* These are used in pastes, mucilages, and fabric sizing.

The acetal linkages of starch are also hydrolyzed when the compound is eaten. Hydrolysis is catalyzed by acids and by enzymes and leads ultimately to the formation of glucose.

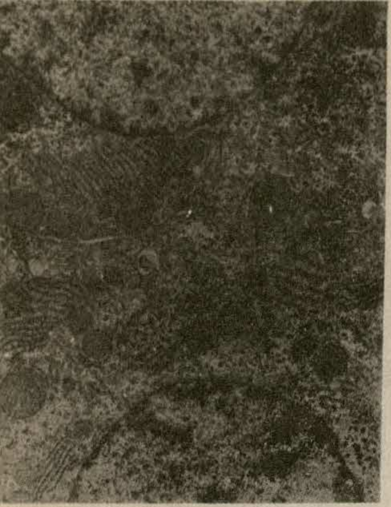
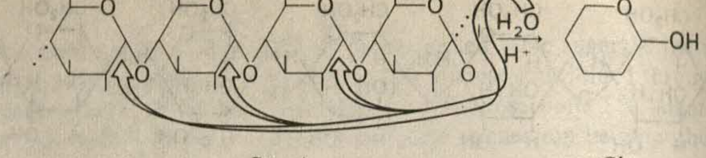


Figure 22.5 Electron micrograph of glycogen granules in a liver cell of a rat. (Photo by Patricia J. Schulz.)



This monosaccharide can be transported by the blood to all parts of the body. Whereas plants store carbohydrates as starch, animals convert glucose to a polymer called *glycogen* for storage in the liver and muscles. Glycogen is similar to amylopectin in structure. In liver and muscle tissue, it is arranged in granules (**figure 22.5**). These granules are clusters of small particles.

Starch is not a reducing sugar. Although there is a hemiacetal function at one end of each molecule, the molecules are so large that the effect of these end groups is too minor to give a visible Tollens', Benedict's, or Fehling's test. Starch is usually detected by its reaction with iodine. The two substances form a complex which is an intense blue-black in concentrated solutions. The test is sensitive enough to detect even minute amounts of starch in solution.

22.9 Cellulose: The Grass Eaters

Like starch, cellulose is a polymer of glucose. It differs, however, in that the glucose units are joined by beta acetal linkages (**figure 22.6**). This may seem to be a minor difference, but its significance is tremendous. Most animals can digest and metabolize starch. People and some other animals get no food value from cellulose. We can eat potatoes, but we can't eat grass. Grazing animals and termites are able to use cellulose, probably due to the action of bacteria in their digestive tracts.

Different linkages also result in different three-dimensional forms for cellulose and starch. For example, cellulose in the cell walls of plants is arranged in *fibrils*—bundles of parallel chains. The fibrils, in turn, are arranged parallel to each other in each layer of the cell wall (**figure 22.7**). Alternate layers have the fibrils running in opposite directions, imparting great strength to the wall.

Cotton fibrils are nearly pure cellulose. These and other cellulosic fibers can be used directly for the spinning of thread and the weaving of fabrics. Alternatively, the fibers can be modified by conversion of the alcohol functions to esters (chapter 21).

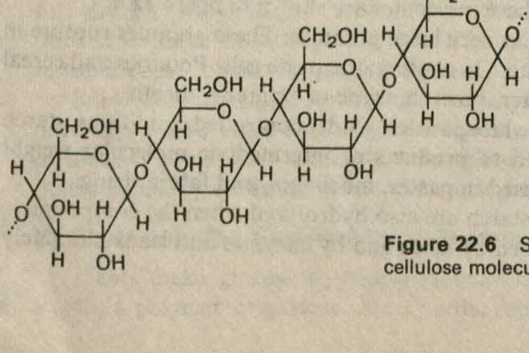


Figure 22.6 Structure of a small segment of a cellulose molecule.

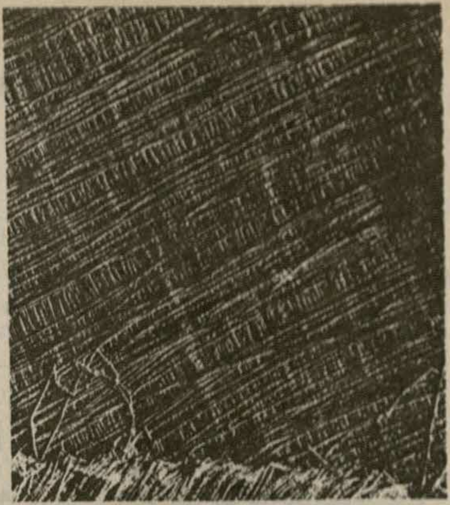


Figure 22.7 Electron micrograph of the cell wall of an alga. The wall consists of successive layers of cellulose fibers in parallel arrangement. (Photo by R. D. Preston, F.R.S., and E. Frei.)

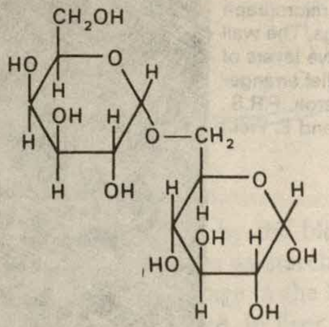
Since so much of the carbon in the biosphere exists as cellulose, considerable research has gone into converting it to glucose or some other form of food for humans. There are enzymes that will degrade cellulose, but to do so efficiently requires some pretreatment of the fibers. Perhaps some day, through the ingenuity of research chemists, we will be able to eat grass and straw—after proper conversion, of course. For the moment we must continue to depend on reactions such as

$$\underset{\text{(grass)}}{\text{Cellulose}} + \text{cow} \longrightarrow \underset{\text{(milk, meat, butter)}}{\text{carbohydrates, proteins, and fats}}$$

Problems

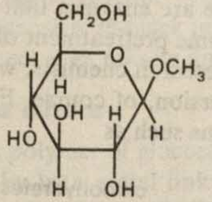
1. Define these terms.
   - a. triose
   - b. aldose
   - c. hexose
   - d. disaccharide
   - e. polysaccharide
   - f. aldopentose
   - g. ketotetrose
   - h. invert sugar
   - i. mutarotation
   - j. glycoside
2. Draw formulas for D-glyceraldehyde and for L-glyceraldehyde. What do the prefixes mean?
3. Draw any ketotetrose and any aldoheptose.
4. From memory, draw formulas for the open-chain forms of D-glucose, D-mannose, D-galactose, and D-fructose.
5. Draw the cyclic structure for α-D-glucose.
6. Knowing that mannose differs from glucose only in the configuration at the second carbon, draw the cyclic structure for α-D-mannose.
7. What monosaccharide(s) are obtained by the hydrolysis of the following?
   - a. starch
   - b. cellulose
   - c. maltose
   - d. lactose
   - e. sucrose
8. Write an equation for the hydrolysis in dilute acid of each of the following.
   - a. a simple acetal
   - b. maltose
   - c. lactose
   - d. sucrose
9. Identify these sugars by their proper names.
   - a. blood sugar
   - b. milk sugar
   - c. cane sugar
   - d. dextrose
   - e. levulose
   - f. invert sugar
   - g. table sugar

10. Melibiose is a disaccharide which occurs in some plant juices. Its structure is



a. What is the monosaccharide unit on the left?
b. What is the monosaccharide unit on the right?
c. What type of linkage (alpha or beta) joins the two rings?
d. Is melibiose a reducing sugar? If so, circle the hemiacetal function and indicate whether it is alpha or beta.

11. The structure of a methyl glycoside of glucose is



a. Is the first carbon in the alpha or the beta configuration?
b. Is the compound a reducing sugar?
c. Will it give a positive test with Tollens' reagent? With Benedict's reagent?

12. What are the essential structural differences between the members of each pair?
a. amylose and amylopectin
b. amylose and cellulose
c. amylose and glycogen

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8. Ternay, Andrew L., Jr., *Contemporary Organic Chemistry*, Philadelphia: W. B. Saunders, 1976. See chapters 4 and 25.

chapter 23

Lipids

The food that we eat is divided into three primary groups: the carbohydrates (chapter 22), the proteins (chapter 24), and the lipids (which we shall discuss in this chapter). The best-known lipids are the fats. These compounds, in our affluent society, often occupy the lowest estate among the three classes of foods. People dieting to lose weight frequently try to eliminate fats from their diet. Gram for gram, fats pack about twice the caloric content of carbohydrates. While that may be bad news for the dieter, it also says something about the efficiency of nature's designs. The body has a very limited capacity for storing carbohydrates. It can tuck away a bit of glycogen in the liver or in muscle tissue, but carbohydrates, primarily in the form of glucose, are meant to serve the body's immediate energy needs. If we intend to store energy reserves, then the more energy we can pack into a given space, the better off we are. The oxidation of fats supplies about 9 kcal/g, whereas the oxidation of carbohydrates supplies only 4 kcal/g. The body, an efficient organism, is geared to store fats, and its capacity for doing so is astounding. There is a recorded instance of a man weighing 486 kg (about 1000 lb). If all that "energy" were stored as carbohydrate, he would have weighed a ton or more (**figure 23.1**).

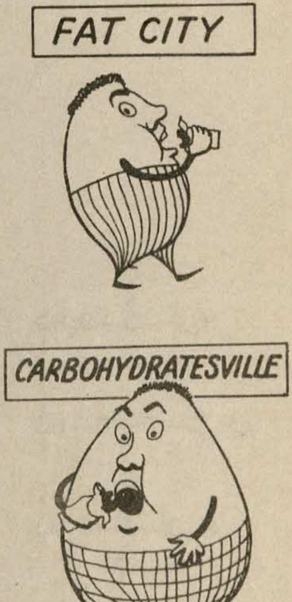


Figure 23.1 It's bad enough to eat too many carbohydrates and get fat, but imagine what would happen if you ate too many fats and got carbohydrate!

The body's ability to store fat may elicit from you feelings of disgust or despair rather than awe. But a quick summary of the other functions of lipids in the body may provide a more positive picture of those essential compounds. They play an important role in brain and nervous tissue. Fats serve as protective padding and insulation for vital organs. Without fats in our diets, we'd be deficient in the fat-soluble vitamins, A, D, E, and K. Most important, lipids make up the major part of the membranes of each of the 10 trillion cells in our bodies.

23.1 What's a Lipid?

Of the three types of foodstuffs, two are classified by functional groups. As we saw in chapter 22, carbohydrates are polyhydroxyaldehydes or ketones.

The proteins, as we shall soon see, are polyamides. But lipids are not polyanythings in particular. They tend to be esters or compounds which can form esters, but that takes in a lot of territory and doesn't even hint at the wide variation in structure found among the lipids.

What makes a lipid a lipid is its solubility. Considering that water is the major solvent in living systems and that reactions of physiological importance tend to take place in aqueous solutions, it is not surprising that insolubility in water should be considered a noteworthy feature when found in important body constituents. Lipids are soluble in relatively nonpolar organic solvents such as carbon tetrachloride, chloroform, and diethyl ether but are generally insoluble in water.

Compounds isolated from body tissues are classified as lipids if they are more soluble in organic solvents than in water. Included in this category are esters of glycerol (an alcohol) and the fatty acids or phosphoric acid; steroids such as cholesterol; compounds which incorporate sugar units or a complicated aminoalcohol called sphingosine; and compounds called prostaglandins, which some regard as potential "miracle" drugs. Because of this broad variation in structure, we can't present a general formula for lipids. We shall, instead, consider one subclass at a time and try to point out similarities and differences in structure as we go along.

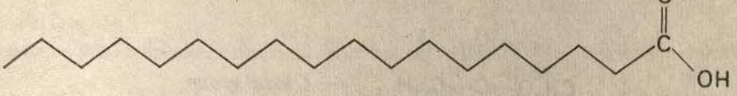
23.2 Fatty Acids Are Long, Skinny Molecules

Fatty acids are so named because they are structural components of fats. Chemically, fatty acids are generally long-chain carboxylic acids. Nearly all contain an even number of carbon atoms. Few are branched. Some, the unsaturated fatty acids, contain one or more double bonds. Free fatty acids are rare, occurring in nature in only small amounts. The fats and other lipids, however, provide a reservoir from which the fatty acids can be obtained. **Table 23.1** lists some common fatty acids and an important source of each of them.

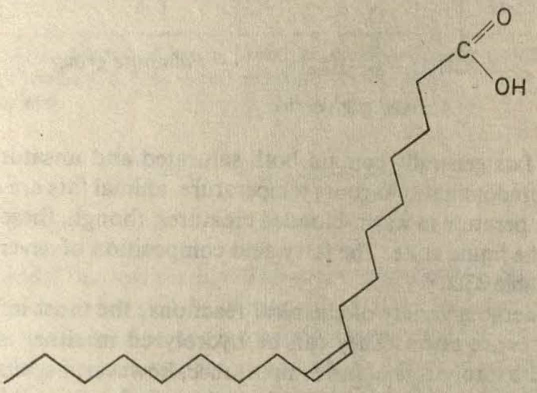
Table 23.1
Some fatty acids in natural fats

Number of Carbon Atoms	*Condensed Structure*	*Name*	*Source*
4	$CH_3CH_2CH_2COOH$	Butyric acid	Butter
6	$CH_3(CH_2)_4COOH$	Caproic acid	Butter
8	$CH_3(CH_2)_6COOH$	Caprylic acid	Coconut oil
10	$CH_3(CH_2)_8COOH$	Capric acid	Coconut oil
12	$CH_3(CH_2)_{10}COOH$	Lauric acid	Palm kernel oil
14	$CH_3(CH_2)_{12}COOH$	Myristic acid	Oil of nutmeg
16	$CH_3(CH_2)_{14}COOH$	Palmitic acid	Palm oil
18	$CH_3(CH_2)_{16}COOH$	Stearic acid	Beef tallow
16	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	Palmitoleic acid	Butter
18	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	Oleic acid	Olive oil
18	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	Linoleic acid	Soybean oil
18	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	Linolenic acid	Linseed oil

The normal tetrahedral bond angles of carbon require that the chain of saturated fatty acid molecules assume a zigzag configuration, but the molecule viewed as a whole is relatively straight.



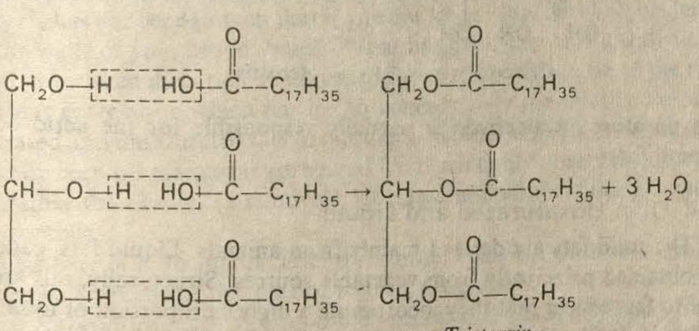
Such molecules fit rather nicely into a crystal lattice, a capability which gives these acids and the fats derived from them relatively high melting points. Unsaturated fatty acids occur almost always in the *cis* configuration. This results in a bend in the molecules.



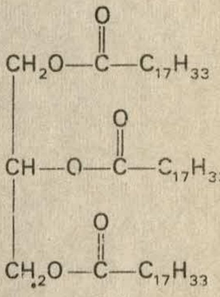
These molecules don't stack neatly; hence, the forces between molecules are smaller. The unsaturated fatty acids and unsaturated fats, consequently, have lower melting points. Most are liquids at room temperature.

23.3 Fats: Solid and Saturated

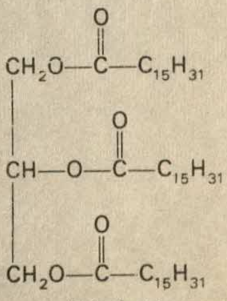
Chemically, fats are esters of the fatty acids and the trihydroxy alcohol glycerol. Three acid units are combined with the three hydroxyl groups in the glycerol molecule. The fatty acid units can be all the same, as in tristearin.



Glycerol *Stearic acid* *Tristearin*

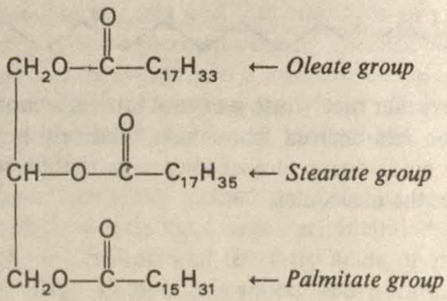


Triolein



Tripalmitin

Fat molecules such as tristearin are called *simple triglycerides*. Other examples are triolein and tripalmitin. Most naturally occurring fats contain different fatty acid units in the same molecule. These are called *mixed triglycerides*. For example, there may be an oleate, a stearate, and a palmitate group present.



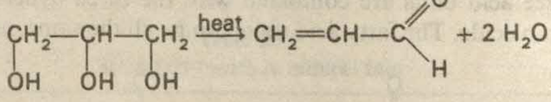
$$\begin{array}{l} CH_2O-\overset{O}{\overset{\|}{C}}-C_{17}H_{33} \\ CH-O-\overset{O}{\overset{\|}{C}}-C_{17}H_{35} \\ CH_2O-\overset{O}{\overset{\|}{C}}-C_{15}H_{31} \end{array}$$

A mixed triglyceride

Animal fats generally contain both saturated and unsaturated fats, but the former predominate. At room temperature, animal fats are usually solids. At body temperature in warm-blooded creatures, though, these fats are likely to exist in the liquid state. The fatty acid composition of several typical fats is given in **table 23.2.**

Fats undergo a variety of chemical reactions; the most important is hydrolysis. Fats are esters. They can be hydrolyzed in either acidic or basic media. Acid hydrolysis is of little importance, however, because it is difficult to dissolve fats in acidic media. Basic hydrolysis is of considerable importance in the making of soap and will be discussed in detail in section 23.5. When we eat fats, they are hydrolyzed by enzymes. This process will be discussed in chapter 31.

When fats are heated, their glycerol portions are dehydrated to acrolein.



$$\underset{OH}{CH_2}-\underset{OH}{CH}-\underset{OH}{CH_2} \xrightarrow{heat} CH_2=CH-C\overset{O}{\underset{H}{\lessgtr}} + 2\,H_2O$$

Glycerol *Acrolein*

This unsaturated aldehyde is partially responsible for the acrid odor of burning fat.

23.4 Oils: Unsaturated and Liquid

The solid fats are derived mainly from animals. Liquid fats, called *oils*, are obtained principally from vegetable sources. Structurally, oils are identical to fats except that they incorporate a higher proportion of unsaturated acid units (**table 23.2**).

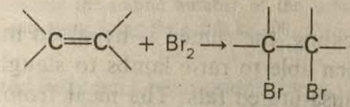
The degree of unsaturation of a fat or an oil is usually measured in terms of the *iodine number*. Recall that halogens such as chlorine and bromine add readily to carbon-carbon double bonds.

Table 23.2

Fatty acid distribution ranges (as percentages) in several fats and oils

Fat or Oil	*Lauric*	*Myristic*	*Palmitic*	*Stearic*	*Oleic*	*Linoleic*	*Others*
Animal fats							
Beef tallow	0.2	2–3	25–30	21–26	39–42	1–3	1.2–1.8*
Lard	—	1	25–30	12–16	41–51	3–8	4.2–8.2*
Butter	1–4	8–13	25–32	8–13	22–29	3	6.6–15.5†
Vegetable oils							
Palm oil	—	1–6	32–47	1–6	40–52	2–11	—
Corn	—	0–2	8–10	1–4	30–50	34–56	1–4*
Soybean	—	0.3	7–11	2–5	22–34	50–60	3–14‡
Cottonseed	—	0–3	17–23	1–3	23–44	34–55	0–1

*Mainly the unsaturated fatty acid having 16 carbon atoms per molecule (palmitoleic acid).
†Mainly the acids having 4, 6, 8, or 10 carbon atoms per molecule.
‡Mainly linolenic acid.



Iodine also adds, but less readily. The iodine number of a fat is the number of grams of iodine that will be consumed by 100 g of fat or oil. The more double bonds a fat contains, the more iodine is required for the addition reaction; thus, a high iodine number means a high degree of unsaturation. Representative iodine numbers are given in **table 23.3.** Notice the generally lower values for the animal fats (butter, tallow, lard) compared to those for the vegetable oils.

The term *polyunsaturated,* often in the news and in advertisements in recent years, simply means that the molecules have several double bonds each. Saturated fats have been implicated, along with cholesterol, a steroid (section 23.9), in one type of arteriosclerosis, hardening of the arteries. As this condition develops, lipids deposit on the walls of arteries. Eventually these deposits become calcified and harden, robbing the vessels of their elasticity. It has *not* been proven that if you eat lots of fats they will be deposited on the walls of your blood vessels. What has been shown is a statistical correlation between diets rich in saturated fats and the incidence of the disease. It is this correlation which has led to concern over the relative amounts of saturated and unsaturated fats in our diets. Advertisers who recommend that you buy corn oil margarine (prepared from relatively unsaturated vegetable oil) rather than butter (a relatively saturated animal fat) take advantage of this concern.

One way of reducing the level of saturated fats is to eat only lean meat. There is also evidence that special feeding programs can produce animals in which the proportions of saturated and unsaturated fats are radically changed. Some grazing animals, such as cattle and sheep, have four-chambered stomachs. It is in the first of these, called the *rumen,* that the unsaturated fatty acids from plants are hydrogenated and become saturated animal fats. In

Table 23.3
Typical iodine numbers for some fats and oils

Fat or Oil	*Iodine Number*
Butter	25– 40
Beef tallow	30– 45
Lard	45– 70
Olive oil	75– 95
Peanut oil	85–100
Cottonseed oil	100–117
Corn oil	115–130
Fish oils	120–180
Soybean oil	125–140
Safflower oil	130–140
Sunflower oil	130–145
Linseed oil	170–205

animals who are suckling, the rumen is bypassed in the digestive process. Researchers have been able to raise lambs to slaughtering age on a milk-based diet high in unsaturated fats. The meat from the lambs showed 10 times as much of the polyunsaturated fats as meat from control animals. The lamb chops were delicious as well as nutritious.

Researchers working in Australia fed steers with a diet supplemented with highly unsaturated safflower oil which had been treated with formaldehyde. The treatment prevented hydrogenation of the unsaturated fats in the rumen. Again, the meat so produced was much higher in polyunsaturated fats. An understanding of the biochemical mechanism of hydrogenation may someday provide us with polyunsaturated lamb chops and beef steaks, courtesy of a group of scientists willing to go roamin' in the rumen.

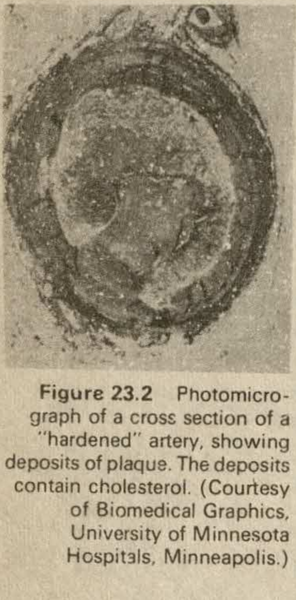


Figure 23.2 Photomicrograph of a cross section of a "hardened" artery, showing deposits of plaque. The deposits contain cholesterol. (Courtesy of Biomedical Graphics, University of Minnesota Hospitals, Minneapolis.)

The hydrogenation of liquid oils to solid fats is not necessarily undesirable, however. Vegetable oils can be converted to solids or semisolids by hydrogenation. Margarine, a butter substitute, and vegetable shortening, a lard substitute, consist of vegetable oils which have been partially hydrogenated. Generally, because of the advertising appeal of polyunsaturated products, the hydrogenation is limited to the degree necessary to give the products the proper consistency. The consumer would get much greater unsaturation by using the oils directly, but most people would rather spread margarine than pour oil on their toast. **Table 23.4** lists iodine numbers for butter and various kinds of margarines.

Recent research has indicated that products of hydrogenation other than saturated fats may be important contributors to arteriosclerosis. According to these studies, *trans* unsaturated isomers, which are rare in natural fats and oils but are formed in the partial hydrogenation of oils, may be the culprits. One thing is certain—much more study in this area is necessary.

On standing at room temperature in contact with moist air, fats and oils soon turn rancid. This rancidity, characterized by disagreeable odors, results from two reactions. Hydrolysis produces volatile fatty acids. Butter, for example, yields foul-smelling butyric, caprylic, and capric acids. Oxida-

Table 23.4
Iodine values and comparative unsaturation ratings of various margarines and butter

Food Product	*Iodine Value*	*Comparative Unsaturation**
Butter	27	100
Margarines		
Hard type A	68	252
Hard type B	72	267
Hard type C	77	285
Soft type D	84	311
Soft type E	88	326
Liquid type F	90	333
Liquid type G	93	344

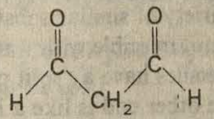
Reprinted with permission from Mancott, Anatol, and Tietjen, John, "Polyunsaturation in Food Products," *Chemistry*, November 1974, p. 29. Copyright © 1974 by the American Chemical Society.

*Calculated by dividing the iodine number of the substance by the iodine number of butter and multiplying the result by 100.

tion of the unsaturated fatty acid components by oxygen in air also produces a variety of volatile, odorous compounds. The structural unit

$$\sim\sim CH{=}CH{-}CH_2{-}CH{=}CH\sim\sim$$

in linoleic and linolenic acids is readily oxidized. One particularly offensive product, formed by the cleavage of both double bonds, is a compound called malonaldehyde.



The stale, sweaty odor of the unwashed skin is due in large part to the oxidation of fats and oils excreted by the body.

23.5 Soap: Suds for You and Your Duds

Animal fats are available in large quantities as a by-product of the meatpacking industry. The fatty acids and many other long-chain organic compounds are derived from these fats. The most important derivatives are soaps. The reaction which converts animal fats to soaps is called, logically, saponification, which we discussed originally as one of the reactions of esters in general (section 18.8). Animal fat is cooked with lye (sodium hydroxide). Glycerol and the sodium salts of the fatty acids are the products. It is the mixture of sodium salts which is called soap. The reaction is illustrated, with tristearin as the fat, in **figure 23.4**.

Soap produced from fat and lye usually contains excess sodium hydroxide, which washing removes. The soap is then molded and cut into bars. Potassium hydroxide is sometimes employed instead of sodium hydroxide.

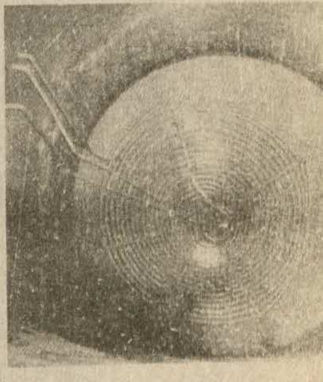


Figure 23.3 Soap is made in large kettles such as this one, which is three stories deep. The kettle is stocked with 59 000 kg of fat and 34 000 kg of lye solution. The yield is about 68 000 kg of soap and 6400 kg of glycerol. (Courtesy of Proctor and Gamble Company, Cincinnati.)

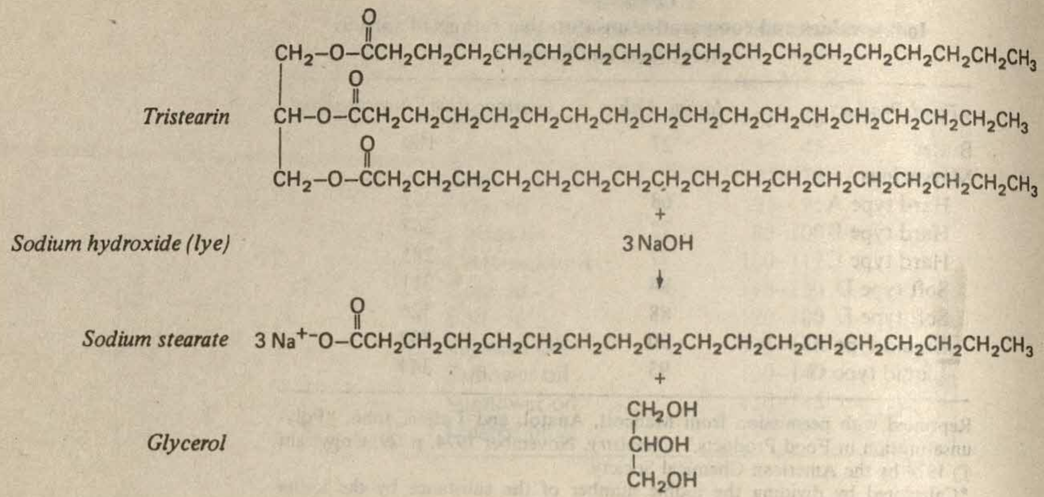


Figure 23.4 Soap is produced by the reaction of animal fat with sodium hydroxide. Tristearin is a fat, and sodium stearate is a soap.

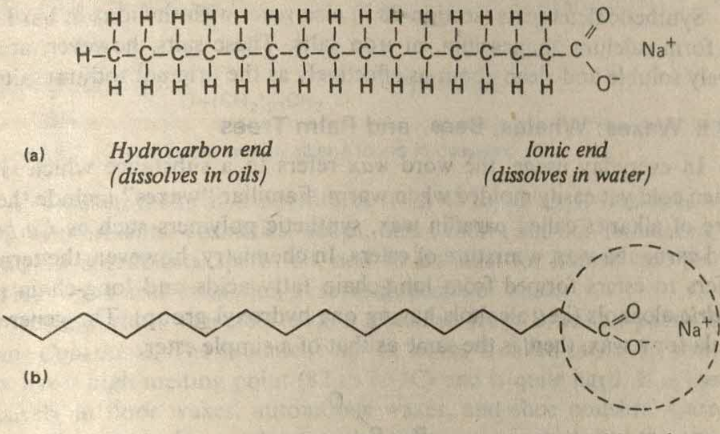
Potassium soaps are softer and produce a finer lather. They are used as liquid soaps and shaving creams. Most soaps contain a number of additives such as perfumes, dyes, and germicides. Scouring soaps contain abrasives to (quite literally) cut grime. Floating soaps have air beaten in before the soap solidifies. This process lowers the density of the bar of soap to less than that of water.

Dirt and grime usually adhere to skin, clothing, and other surfaces bebecause they are combined with greases and oils—body oils, cooking fats, lubricating greases, or a variety of similar substances—which act a little like sticky glues. Since oils are not miscible with water, washing with water alone does little good. Soap molecules have a "split personality." One end is ionic and dissolves in water. The other end is like a hydrocarbon and dissolves in oils (**figure 23.5**). If we represent the ionic end of the molecule as a circle and the hydrocarbon end as a zigzag line, we can illustrate the cleansing action of soap schematically (**figure 23.6**). The hydrocarbon "tails" stick into the oil. The ionic "heads" remain in the aqueous phase. In this manner the oil is broken into tiny droplets and dispersed throughout the solution. The droplets don't coalesce, because of the repulsion of the charged groups (the carboxyl anions) on their surfaces. The oil and water form an emulsion, with soap acting as the emulsifying agent. With the oil no longer "gluing" it to the surface, the dirt can be easily removed.

For cleaning clothes and for many other purposes, soap has been largely replaced by synthetic detergents because soaps have two rather serious shortcomings. One of these is that, in acidic solutions, soaps are converted to free fatty acids.

$$\begin{array}{ll} \textit{A soap} & CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2COO^-Na^+ \\ & \qquad\qquad\qquad\qquad\qquad\qquad\qquad \downarrow H^+ \\ \textit{A fatty acid} & CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2COOH \end{array}$$

Figure 23.5 Sodium palmitate, a soap. (a) Structural formula. (b) A schematic representation.



(a)
Hydrocarbon end (dissolves in oils)
Ionic end (dissolves in water)
(b)

The fatty acids, unlike soap, don't have an ionic end. Lacking the necessary "split personality," they can't emulsify the oil and dirt; that is, they do not exhibit any detergent action. What is more, these fatty acids are insoluble in water and would thus precipitate as a greasy scum. To counteract this lack of detergent action in acidic solution, various alkaline substances are added to laundry soap formulations to keep the pH high. These basic compounds include carbonates, phosphates, and silicates.

The second serious disadvantage of soap is that it doesn't work very well in hard water. Hard water is just water which contains certain metal ions, particularly magnesium, calcium, and iron ions. The soap anions react with these metal ions to form greasy, insoluble curds.

$$\underbrace{2\,CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2COO^-Na^+}_{\text{Soap (soluble)}} + Ca^{2+} \longrightarrow$$

$$\underbrace{(CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2COO^-)_2Ca^{2+}}_{\text{Bathtub ring (insoluble)}} + 2\,Na^+$$

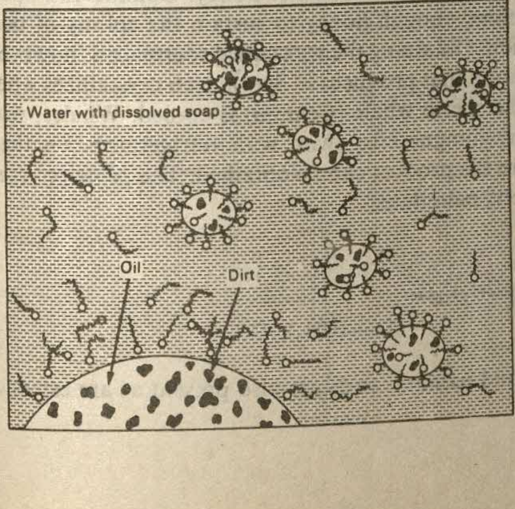


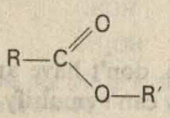
Figure 23.6 The action of soap in removing dirt.

These deposits make up the familiar bathtub ring. They leave freshly washed hair sticky and are responsible for the "telltale gray" of the family wash.

Synthetic detergents (section 20.7) also react with the ions in hard water to form calcium, magnesium, or iron salts. These salts, however, are relatively soluble and clean about as effectively as the original sodium salts.

23.6 Waxes: Whales, Bees, and Palm Trees

In everyday usage, the word *wax* refers to a substance which is hard when cold yet easily molded when warm. Familiar "waxes" include the mixture of alkanes called paraffin wax, synthetic polymers such as *Carbowax*, and carnauba wax, a mixture of esters. In chemistry, however, the term *wax* refers to esters formed from long-chain fatty acids and long-chain *monohydric* alcohols (i.e., alcohols having one hydroxyl group). The general formula for a wax, then, is the same as that of a simple ester.

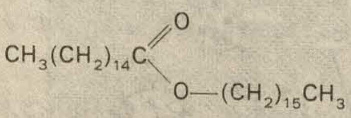


For a wax, however, R and R′ are limited to alkyl groups containing a large number of carbon atoms.

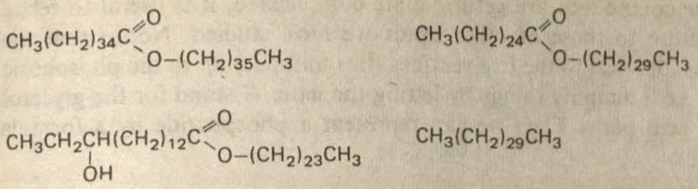
Most natural waxes are mixtures of such esters. Many also contain free alcohols, hydrocarbons, and esters of dibasic acids, hydroxy acids, and diols. All have similar properties; they feel "waxy," are insoluble in water, and melt at temperatures above body temperature (37 °C) and below the boiling point of water (100 °C).

Beeswax is the material from which bees construct honeycombs. Upon saponification, beeswax yields alcohols and fatty acid salts with even numbers of carbon atoms. The alcohols generally have 24 to 36 carbon atoms. The fatty acids have up to 36 carbon atoms; about one-fourth are hydroxy acids. About 20% of beeswax is hydrocarbons. These have odd numbers of carbon atoms from 21 to 33. **Figure 23.7** shows some of the typical molecules found in beeswax.

Beeswax is a by-product of the production of honey. Commercial operations can always leave behind enough honey to sustain the colony of bees and ensure future production. Obtaining the wax called spermaceti, however, is a little harder on the creature that produces it. Spermaceti crystallizes when the oil from the head of the sperm whale (*Cetacea*) is cooled. Whales, who are notorious for their unwillingness to swim with refrigerators on their heads, must be killed before the product can be obtained. The principal constituent of spermaceti is cetyl palmitate.



Esters of lauric, myristic, and palmitic acids are also present as are esters of higher alcohols.



$CH_3(CH_2)_{34}COO(CH_2)_{35}CH_3$ $CH_3(CH_2)_{24}COO(CH_2)_{29}CH_3$

$CH_3CH_2CH(OH)(CH_2)_{12}COO(CH_2)_{23}CH_3$ $CH_3(CH_2)_{29}CH_3$

Figure 23.7 Three esters and an alkane found in beeswax.

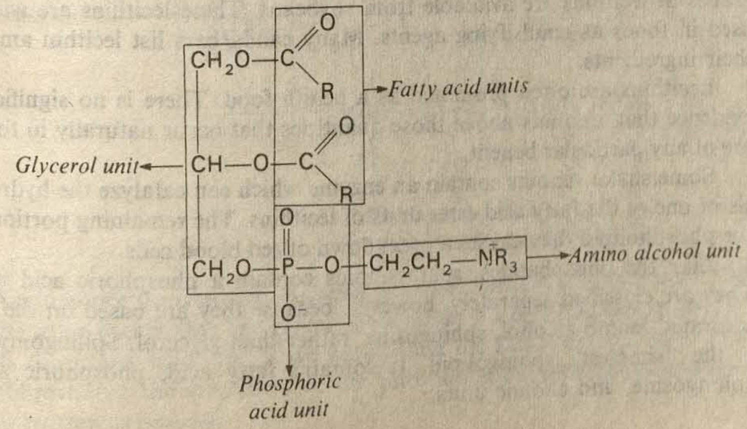
Spermaceti melts at temperatures from 42 to 50 °C. It was once widely used in ointments, cosmetics, soaps, and candles and for laundering. Demand for spermaceti, sperm oil, and whale meat for human and pet food has led to the near extinction of several species of whale.

An important vegetable wax is obtained from Brazilian palms of the genus *Copernicia*. The exudate from the leaves is called carnauba wax. This wax has a high melting point (82 to 86 °C) and is quite hard. It is used extensively in floor waxes, automobile waxes, and shoe polishes. Carnauba wax is thought to be a polyester, the monomer of which has the structure $HO(CH_2)_nCOOH$, where n is an odd number from 17 to 29.

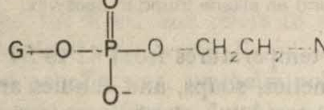
Many natural waxes have been replaced by synthetic materials, mainly polymers. By careful control of the molecular weight, the properties of natural waxes can be closely duplicated. For example, *Carbowax*, a polymer of ethylene glycol ($HO{-}CH_2CH_2{-}OH$), is available in a range of average molecular weights. Synthetic waxes are used in cosmetics and ointments and in certain industrial processes.

23.7 Phospholipids: Brains and Eggs

Glycerol is an alcohol. It forms esters with acids. When the acids are carboxylic acids, the esters formed are fats. But glycerol can also form esters with inorganic acids, such as phosphoric acid. The phosphatides, a most important class of phospholipids (phosphorus-containing lipids), are esters of glycerol in which there are two fatty acid groups and one phosphoric acid residue. Further, the phosphoric acid is also esterified with another alcohol molecule, usually an amino alcohol.



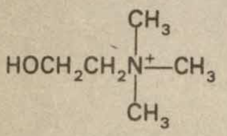
Since these compounds are getting quite complicated, it is useful to relate their structure to those of other lipids we have studied. Notice that the molecule is identical to the triglycerides (fats and oils) up to the phosphoric acid part. Let's simplify things by letting the letter *G* stand for the glycerol and fatty acid parts. Then we can represent a phosphatide by a formula such as



$$G{-}O{-}\overset{\overset{\large O}{\|}}{\underset{\underset{\large O^-}{|}}{P}}{-}O{-}CH_2CH_2{-}NR_3$$

HO—$CH_2CH_2NH_2$

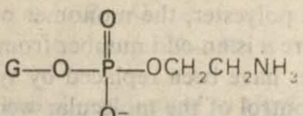
Ethanolamine (2-aminoethanol)



$$HOCH_2CH_2\overset{\overset{\large CH_3}{|}}{\underset{\underset{\large CH_3}{|}}{N^+}}{-}CH_3$$

Choline

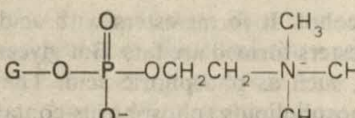
Two of the amino alcohols incorporated in phosphatides are ethanolamine and choline. When the phosphatide contains the *ethanolamine* structural group (we've shown the amine group ionized), the compounds are called *cephalins*.



$$G{-}O{-}\overset{\overset{\large O}{\|}}{\underset{\underset{\large O^-}{|}}{P}}{-}OCH_2CH_2NH_3$$

The cephalins are found in brain tissue and nerves. They are also involved in blood clotting.

When *choline* is the amino alcohol unit, the compounds are called *lecithins*.



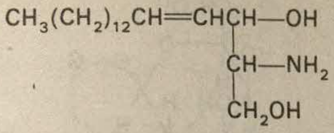
$$G{-}O{-}\overset{\overset{\large O}{\|}}{\underset{\underset{\large O^-}{|}}{P}}{-}OCH_2CH_2{-}\overset{\overset{\large CH_3}{|}}{\underset{\underset{\large CH_3}{|}}{N}}{-}CH_3$$

Lecithins occur in all living organisms. They, too, are important constituents of nerve and brain tissue. Eggs are especially rich in lecithins. Commercial grades of lecithins are available from soybeans. These lecithins are widely used in foods as emulsifying agents. Many candy bars list lecithin among their ingredients.

Lecithins are often promoted as a health food. There is no significant evidence that amounts above those quantities that occur naturally in foods are of any particular benefit.

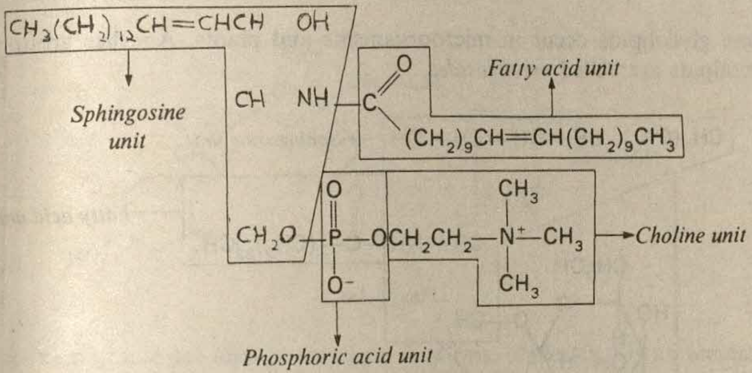
Some snake venoms contain an enzyme which can catalyze the hydrolysis of one of the fatty acid ester units of lecithins. The remaining portion of the phospholipid then causes a breakdown of red blood cells.

Like the phosphatides, sphingolipids contain a phosphoric acid unit. They are classified separately, however, because they are based on the unsaturated amino alcohol, sphingosine, rather than glycerol. Sphingomyelin is the "simplest" sphingolipid. It contains fatty acid, phosphoric acid, sphingosine, and choline units.



$$\begin{array}{l} CH_3(CH_2)_{12}CH{=}CHCH{-}OH \\ \qquad\qquad\qquad\qquad\quad | \\ \qquad\qquad\qquad\qquad\quad CH{-}NH_2 \\ \qquad\qquad\qquad\qquad\quad | \\ \qquad\qquad\qquad\qquad\quad CH_2OH \end{array}$$

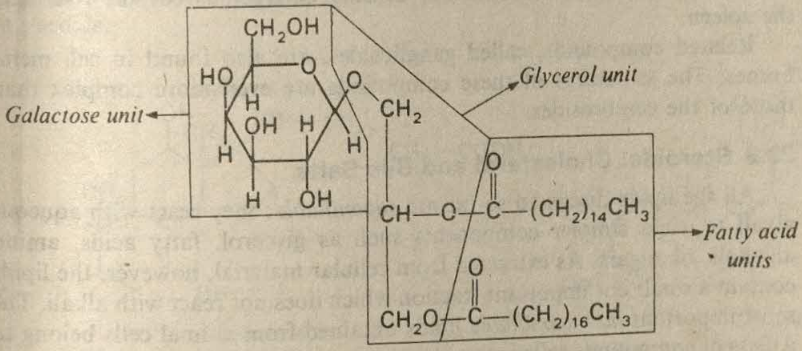
Sphingosine



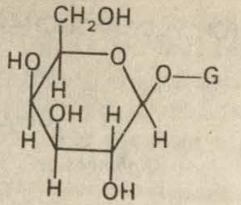
A sphingomyelin

Sphingomyelins are important constituents of the myelin sheath that surrounds the axon of a nerve cell. Multiple sclerosis is one of several diseases related to a fault in the myelin sheath.

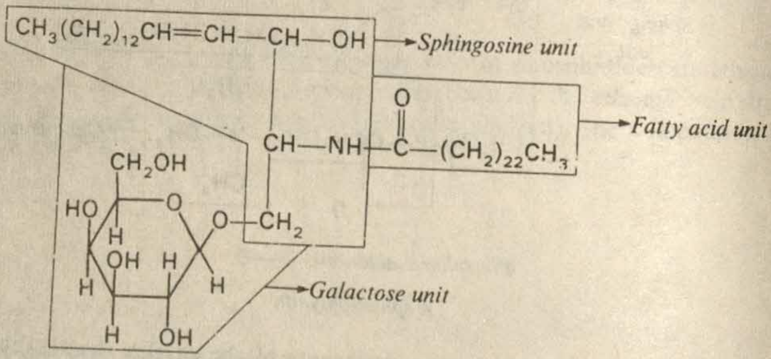
Glycolipids may incorporate glycerol or sphingosine, fatty acids, and, always, a sugar unit. They contain no phosphoric acid. The simplest contain two fatty acid units and one sugar unit, such as a galactose unit, combined with glycerol.



Again notice the similarity between this molecule and a fat molecule. They're the same except that the glycolipid attaches a sugar unit where the fat has its third fatty acid unit. If we were to use the same convention we used in abbreviating the structures of the phospholipids, these glycolipids would be written as follows.



These glycolipids occur in microorganisms and plants. Another group of glycolipids are called *cerebrosides.*



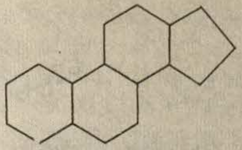
These contain a galactose unit, a fatty acid unit, and a sphingosine unit. The cerebrosides qualify not only as glycolipids but also as sphingolipids. The structure resembles that of a sphingomyelin, except that a sugar unit is connected where the sphingomyelin has a choline phosphate group. The cerebrosides are important constituents of the membranes of nerve and brain cells. Gaucher's disease, a hereditary affliction, results from the substitution of glucose for galactose in the cerebroside. Large amounts of these abnormal cerebrosides accumulate, causing enlargement of the liver and the spleen.

Related compounds, called gangliosides, are also found in cell membranes. The structures of these compounds are even more complex than those of the cerebrosides.

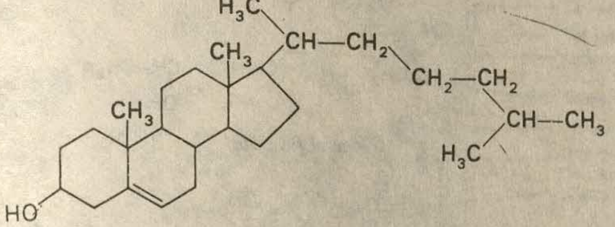
23.9 Steroids: Cholesterol and Bile Salts

All the lipids discussed so far are *saponifiable;* they react with aqueous alkali to yield simpler components such as glycerol, fatty acids, amino alcohols, or sugars. As extracted from cellular material, however, the lipids contain a small but important fraction which does not react with alkali. The most important *nonsaponifiable* lipids obtained from animal cells belong to a class of compounds called *steroids*. These compounds include the bile salts, cholesterol and related compounds, hormones such as cortisone, and the all-important sex hormones. Those steroids with hormonal activity will be discussed in detail in chapter 27.

All steroids have a common structural unit—a system of four fused rings. Three rings have six members each; the fourth has only five carbons.



The most abundant of the steroids is cholesterol.



Cholesterol

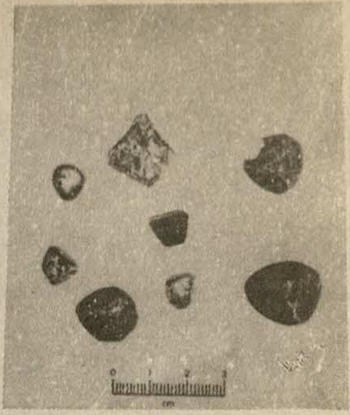
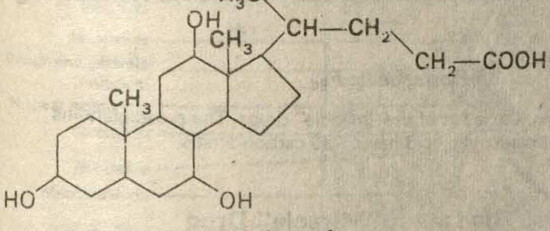


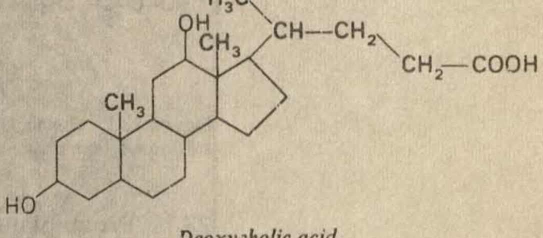
Figure 23.8 Gallstones are often composed largely of cholesterol. (Courtesy of Biomedical Graphics, University of Minnesota Hospitals, Minneapolis.)

As its name indicates and its structure confirms, cholesterol is an alcohol. However, its 27 carbon atoms are more than enough to establish its hydrocarbon character, including its solubility in nonpolar solvents. Cholesterol is a common component of all animal tissues. The brain is about 10% cholesterol, but the function of cholesterol there is unknown. Cholesterol is a major component of certain types of gallstones. It is also found in the lipid deposits in hardened arteries, although it has not been established whether it is there as a cause of hardening of the arteries or as an effect from some other process.

Bile is a fluid which is formed in the liver and stored in the gallbladder. It is released from time to time into the digestive tract, where it aids in the digestion of fats (chapter 29). The bile salts are the principal active ingredients of bile. They are derived from cholic acid and deoxycholic acid, which are steroids.

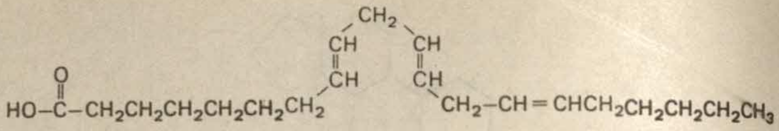


Cholic acid

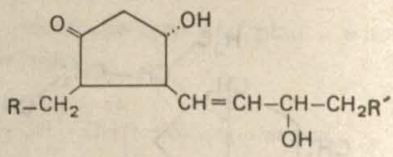


Deoxycholic acid

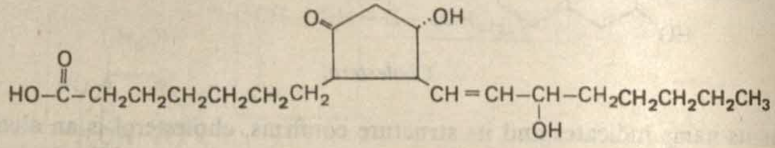
The bile salts derived from these compounds have an ionic portion and a less polar portion. They are emulsifying agents, acting much like soap as they break up fats into tiny particles and suspend them in the body's aqueous solutions. The emulsified fats are much more readily digested and more easily transported.



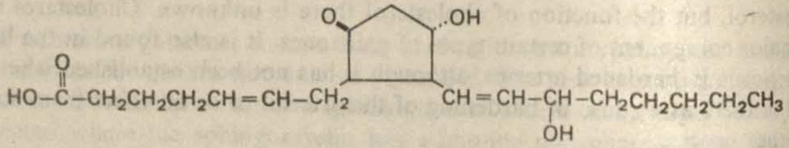
Unsaturated carboxylic acid



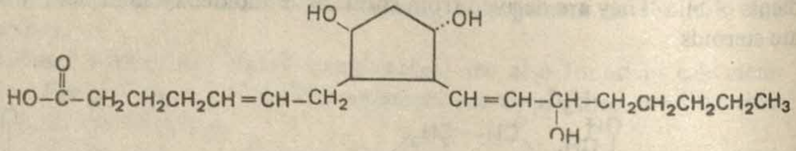
General formula



Prostaglandin E_1



Prostaglandin E_2



Prostaglandin F_{2a}

Figure 23.9 Prostaglandins, the latest of the "miracle" drugs. The prostaglandins are derived from unsaturated carboxylic acid having 20 carbon atoms.

23.10 Prostaglandins: The Latest "Miracle" Drug

Perhaps no compounds since the development of birth control pills have aroused as much activity among pharmaceutical companies as have the group of compounds called *prostaglandins*. Biochemically, prostaglandins are derived from a fatty acid with 20 carbon atoms (**figure 23.9**). There are six primary prostaglandins; many others have been identified. These compounds are widely distributed throughout the body, but at extremely low concentrations. They are among the most potent biological chemicals, eliciting marked changes with extremely small doses.

In some respects, the prostaglandins act much as hormones do, regulating such things as smooth muscle activity, blood flow, and secretion of various substances. This range of physiological activity led to claims that, as drugs,

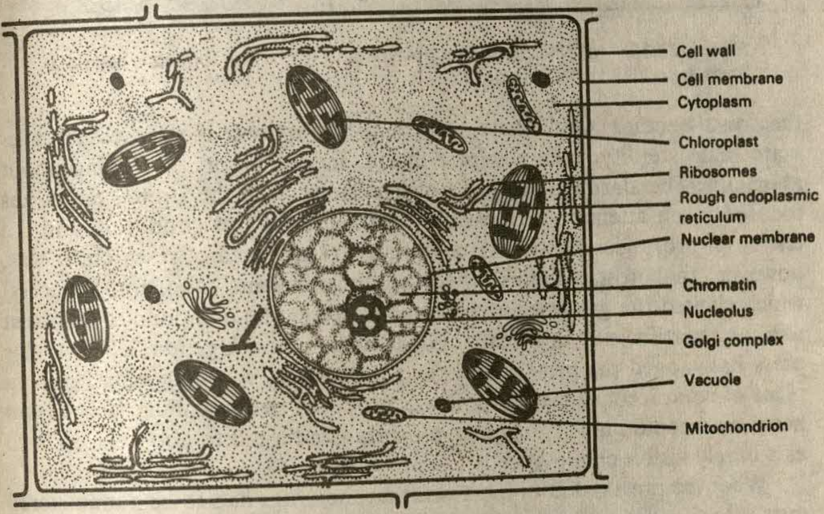


Figure 23.10 An idealized "typical" plant cell.

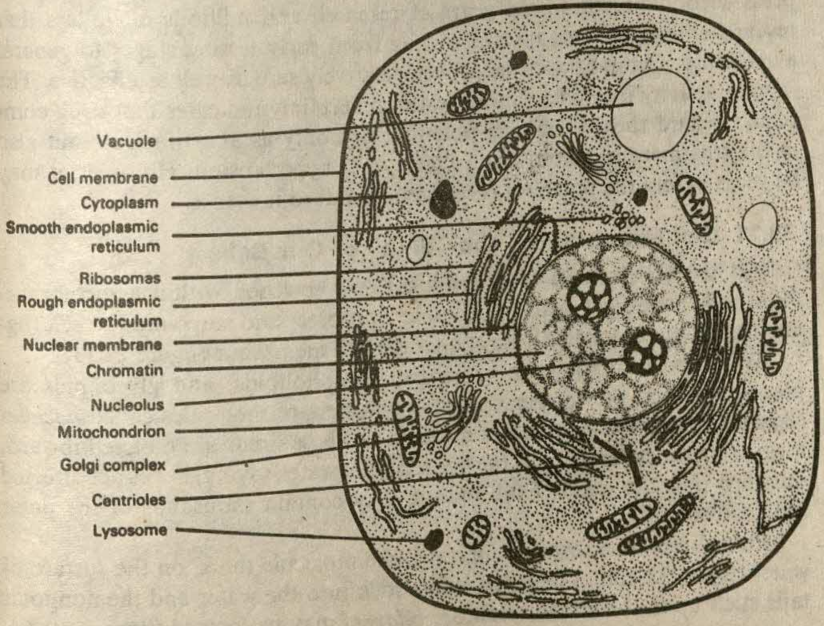


Figure 23.11 An idealized "typical" animal cell.

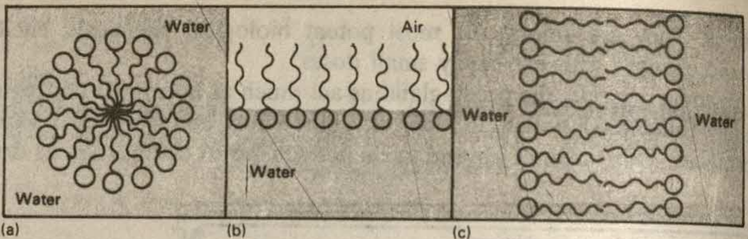


Figure 23.12 (a) Micelle, (b) monolayer, and (c) bilayer formed when polar lipids are added to the water.

the prostaglandins could relieve nasal congestion, lower blood pressure, alleviate male sterility, relieve peptic ulcers, induce labor, and bring about abortions. The alarming incidence of hypertension in the United States has focused much attention on possible treatments for this condition, and the testing of prostaglandins is one potentially fruitful area of research. It was, however, the prostaglandins' effect as abortifacients (abortion inducers) which elicited the greatest initial public interest. The compounds had been used as abortifacients in Sweden, Great Britain, and Uganda. The popular press ballyhooed the prostaglandins as a possible "morning after" pill. In place of contraceptive measures, it was proposed that a woman who missed her period could immediately take a prostaglandin pill to abort the embryo as a barely visible clump of cells.

What the press did not report was that the drugs had to be administered over a long period of time—8 to 14 hours—by infusion. Far from being a "morning after" *pill*, the drugs had to be injected from a bottle through a needle into a vein, in the same way a patient is given blood. Neither did the press accounts mention the years of research and millions of dollars that researchers would need to take a drug from early testing stages to general availability. Drugs have to be proven relatively safe as well as effective. The intense activity in prostaglandin research certainly indicates that drug companies regard them as having potential not only as abortifacients but also in the treatment of emphysema, ulcers, and hypertension. However, it may be years before the potential is realized, if indeed it ever is.

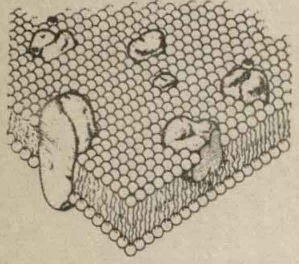


Figure 23.13 A cell membrane model showing proteins in a lipid bilayer. (Reprinted with permission from Chapwick, Philip, "The Skin of Our Cells," *The Sciences*, April 1973. Copyright © 1973 by the New York Academy of Sciences.)

23.11 Cell Membranes: The "Skin" of Our Cells

All the components of a living cell are enclosed within a membrane. Plant cells have rigid walls of cellulose to protect and surround the cell (**figure 23.10**), but animal cells have only the cell membrane (**figure 23.11**).

When polar lipids such as soaps, phospholipids, and glycolipids are placed in water, they disperse, forming clusters of molecules called *micelles* (**figure 23.12a**). The hydrocarbon "tails" of these lipids are directed inward, away from the polar solvent; the hydrophilic (water-loving) heads are directed outward into the water. Each micelle may contain thousands of the polar lipid molecules.

Polar lipids also form *monolayers*, one molecule thick, on the surface of water (**figure 23.12b**). The polar heads stick into the water and the nonpolar tails stick up in the air. In addition, *bilayers* may be formed (**figure 23.12c**), with the hydrophobic (water-fearing) tails sandwiched between the hydrophilic heads sticking outward into the water. These bilayers have properties quite similar to those of cell membranes.

In addition to lipids, cell membranes contain protein molecules. It is quite likely that these proteins are involved in the *active transport* of materials through the cell membrane; that is, they are not simply passive structural material but somehow actively assist substances moving into and out of cells. The proteins seem not only to coat the outside of a lipid bilayer but also to line "holes" through which molecules pass into and out of the cell (**figure 23.13**). Various proteins pass different substances preferentially. For example, one type of protein may transport potassium ions, while another may preferentially pass sodium ions. This model of cell membranes is a tentative one. It may well be modified as research continues in this exciting area.

Problems

1. Define and illustrate or give an example of each of the following.
    a. lipid
    b. fatty acid
    c. simple triglyceride
    d. mixed triglyceride
    e. fat
    f. oil
    g. polyunsaturated oil
    h. iodine number
    i. soap
    j. wax
    k. phospholipid
    l. sphingolipid
    m. glycolipid
    n. phosphatide
    o. lecithin
    p. cephalin
    q. cerebroside
    r. steroid
    s. prostaglandin
    t. saponifiable lipid
    u. nonsaponifiable lipid
    v. micelle
    w. monolayer
    x. bilayer
2. Write a structural formula for each of these.
    a. glyceryl tristearate (tristearin)
    b. octadecyl palmitate
    c. sodium oleate
    d. calcium myristate
    e. linoleic acid
    f. linolenic acid
3. Which would you expect to have a higher iodine number—corn oil or beef tallow? Explain your reasoning.
4. Which would you expect to have the higher iodine number—hard or liquid margarine? Explain your reasoning.
5. What are two ways in which butter can go rancid?
6. Explain how soap acts as a cleaning agent.
7. What are the two main disadvantages of soap? Write an equation to illustrate each.
8. Why does hard water not deactivate a synthetic detergent?
9. What fat would be formed by the complete hydrogenation of triolein? Of trilinolein?
10. Write an equation for the saponification of triolein.
11. Classify the following as saponifiable or nonsaponifiable lipids.
    a. tristearin
    b. cholesterol
    c. a lecithin
    d. a prostaglandin
12. Which of the following are derived from glycerol, which from sphingosine, and which from neither?
    a. fats
    b. oils
    c. waxes
    d. phosphatides
    e. steroids
    f. cerebrosides
    g. prostaglandins

13. Which of the following contain phosphate units?
    a. fats
    b. oils
    c. waxes
    d. phosphatides
    e. steroids
    f. cerebrosides
    g. prostaglandins
    h. glycolipids
14. Draw the basic steroid skeleton.
15. Relate the action of the bile acids to that of soap.
16. List some possible future uses of prostaglandin drugs.

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chapter 24

Amino Acids and Proteins

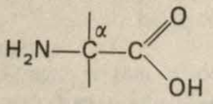
Carbohydrates, lipids, and proteins—the three classes of foods. All are essential to life, but proteins perhaps are closest to the stuff of life itself. No living part of the human body—nor of any other organism, for that matter—is completely without protein. There is protein in the blood, in the muscles, in the brain, and even in tooth enamel. The smallest cellular organisms, the bacteria, contain protein. And the viruses, so small that they make the bacteria look like giants, are nothing but large molecules of conjugated proteins—nucleoproteins. Nucleoproteins are combinations of proteins with nucleic acids. Nucleic acids (chapter 25) cause proteins to be formed, and through these proteins they control the structure and function of cells.

Each type of cell makes its own specific kinds of proteins. Proteins serve as structural material for animals, much as cellulose does for plants. Muscle tissue is largely protein. So are skin and hair. Proteins are made in different forms in different animals: silk, wool, nails, claws, feathers, horns, and hoofs are all proteins.

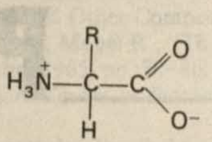
In an overcrowded, hungry world, protein is of increasing importance. The rich nations have it—in the form of beef steak, fish, fowl, soybeans. The poor nations need it but can't afford it. A nation's consumption of sulfuric acid has long been considered an indication of its industrial development. Perhaps its consumption of protein is a better indication of the quality of life of its people, for without protein no nation can have the healthy, vigorous people who are vital to progress. The last major wars were fought over land and mineral resources. The next wars may well be fought over proteins—or over the nitrates, phosphates, and energy needed to produce them.

24.1 Amino Acids: Structure and Physical Properties

Proteins are copolymers of up to 26 different monomers. The monomers are all alpha amino acids. These compounds contain two functional groups, a carboxyl group (—COOH) and an amino group (—NH_2). The amino group is always bonded to the carbon atom alpha to the carboxyl group.

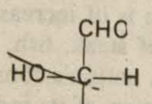


The partial formula indicates the proper placement of these groups, but the structure is not really correct. Acids react with bases to form salts; the carboxyl group is acidic and the amino group is basic. Therefore, these two functional groups interact, the acid transferring a proton to the base. The resulting product is an inner salt or *zwitterion,* a compound in which the anion and cation are part of the same molecule.

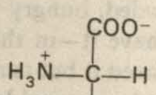


The structure is also referred to as a dipolar ion. While amino acids sometimes are written as un-ionized structures, their physical properties suggest that they actually exist in the ionized form. They are crystalline solids at room temperature. Indeed, attempts to take melting points result in decomposition rather than melting, with charring generally occurring above 200 °C. Water solubility varies but is generally greater than solubility in nonpolar organic solvents such as chloroform and benzene. These properties are consistent with a zwitterion structure. We shall, therefore, ordinarily draw amino acids as zwitterions.

What makes one alpha amino acid different from another is the identity of the "R" group, which is also attached at the alpha position. If this R group is anything other than hydrogen, the amino acid exists in the form of mirror image isomers. Nearly all naturally occurring amino acids have the L configuration. Note the similarity in the configurations of L-glyceraldehyde and the amino acid L-serine.



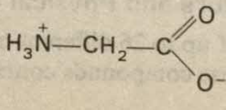
L-Glyceraldehyde



L-Serine

24.2 Introducing Some Interesting Amino Acids

The simplest alpha amino acid is glycine, in which the R group is a hydrogen.



Several amino acids have simple **hydrocarbon** side chains. These include alanine (in which the R group is methyl), phenylalanine (in which the R group is $C_6H_5CH_2$), valine (in which the R group is isopropyl), leucine (in which the R group is isobutyl), and isoleucine (in which the R group is *sec*-butyl). Structures of these and other amino acids are given in **table 24.1.**

Table 24.1
Amino acids that occur naturally in proteins

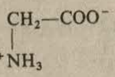
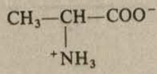
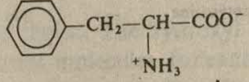
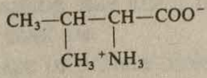
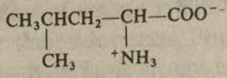
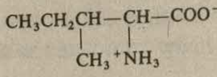
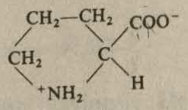
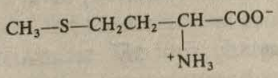
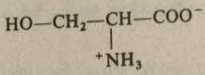
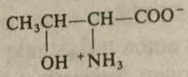
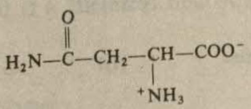
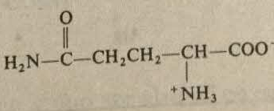
Name	*Abbreviation*	*Essential*	*Structure*
Nonpolar side chains			
Glycine	Gly	No	 $\underset{{}^{+}NH_3}{CH_2}-COO^-$
Alanine	Ala	No	 $CH_3-\underset{{}^{+}NH_3}{CH}-COO^-$
Phenylalanine	Phe	Yes	
Valine	Val	Yes	 $CH_3-\underset{CH_3}{CH}-\underset{{}^{+}NH_3}{CH}-COO^-$
Leucine	Leu	Yes	 $CH_3\underset{CH_3}{CH}CH_2-\underset{{}^{+}NH_3}{CH}-COO^-$
Isoleucine	Ile	Yes	 $CH_3CH_2\underset{CH_3}{CH}-\underset{{}^{+}NH_3}{CH}-COO^-$
Proline	Pro	No	
Methionine	Met	Yes	 $CH_3-S-CH_2CH_2-\underset{{}^{+}NH_3}{CH}-COO^-$
Polar, but not ionizable, side chains			
Serine	Ser	No	 $HO-CH_2-\underset{{}^{+}NH_3}{CH}-COO^-$
Threonine	Thr	Yes	 $CH_3\underset{OH}{CH}-\underset{{}^{+}NH_3}{CH}-COO^-$
Asparagine	Asn	No	 $H_2N-\overset{O}{\overset{\|}{C}}-CH_2-\underset{{}^{+}NH_3}{CH}-COO^-$
Glutamine	Gln	No	 $H_2N-\overset{O}{\overset{\|}{C}}-CH_2CH_2-\underset{{}^{+}NH_3}{CH}-COO^-$

Table 24.1 (continued)

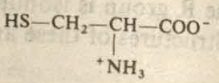
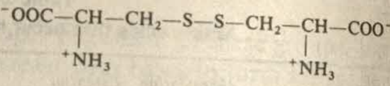
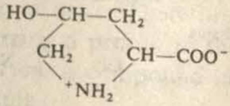
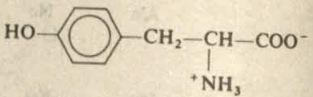
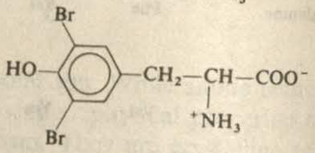
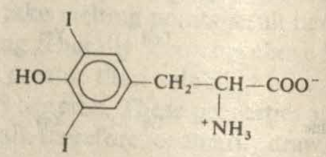
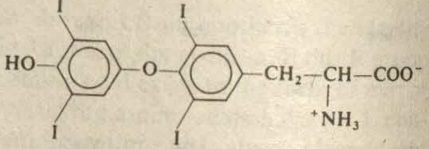
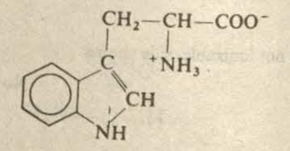
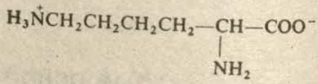
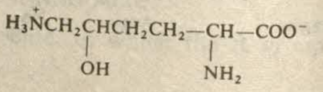
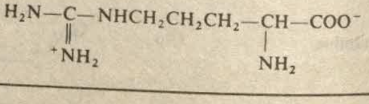
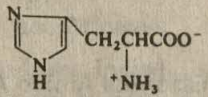
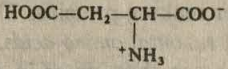
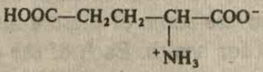
Name	*Abbreviation*	*Essential*	*Structure*
Cysteine	Cys	No	 $HS-CH_2-\underset{^+NH_3}{CH}-COO^-$
Cystine	Cys—SS—Cys	No	 $^-OOC-\underset{^+NH_3}{CH}-CH_2-S-S-CH_2-\underset{^+NH_3}{CH}-COO^-$
Hydroxyproline	Hyp	No	
Tyrosine	Tyr	No	
3,5-Dibromotyrosine	—	No	
3,5-Diiodotyrosine	—	No	
Thyroxine	—	No	
Tryptophan	Try	Yes	
Basic side chains, ionizable			
Lysine	Lys	Yes	 $H_3\overset{+}{N}CH_2CH_2CH_2CH_2-\underset{NH_2}{CH}-COO^-$
Hydroxylysine	Hyl	No	 $H_3\overset{+}{N}CH_2\underset{OH}{CH}CH_2CH_2-\underset{NH_2}{CH}-COO^-$
Arginine	Arg	*	 $H_2N-\underset{^+NH_2}{\overset{}{C}}-NHCH_2CH_2CH_2-\underset{NH_2}{CH}-COO^-$

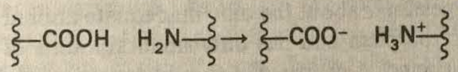
Table 24.1 (continued)

Name	*Abbreviation*	*Essential*	*Structure*
Histidine	His	—†	
Acidic side chains, ionizable			
Aspartic acid	Asp	No	 $HOOC—CH_2—\underset{^{+}NH_3}{CH}—COO^-$
Glutamic acid	Glu	No	 $HOOC—CH_2CH_2—\underset{^{+}NH_3}{CH}—COO^-$

*Essential to growing children but not to adult humans.
†Essential to rats but not to humans.

Several amino acids contain polar side chains. The hydroxyl groups in serine, threonine, hydroxyproline, and tyrosine molecules, for example, may be involved in hydrogen bonding. Such bonding may affect the shape of protein molecules in important ways, as we shall see.

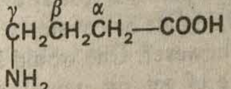
Perhaps even more important to the shape of protein molecules is the presence of ionizable groups in the side chains of certain amino acids. Aspartic and glutamic acid have acidic groups in their side chains. Four others—histidine, lysine, hydroxylysine, and arginine—have basic groups in their side chains. These groups are ionizable. If the amino acids containing them are incorporated into a protein, a proton transfer can occur when the groups are brought into close contact.



$$—COOH \quad H_2N— \rightarrow —COO^- \quad H_3N^{+}—$$

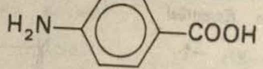
This is exactly the same acid-base reaction given previously. Here, however, it is the side chains which are interacting and not the amino and acid groups which give the amino acids, as a class, their name. The ionic charges which result from side chain interactions, because of their strong attraction for one another, contribute markedly to the structure of some proteins. Such interactions are called salt bridges.

In addition to the 26 alpha amino acids derived from proteins, there are many other amino acids of physiological importance which are not derived from proteins. Most have been isolated from plants, but some are found in animals. For example, γ-aminobutyric acid is a chemical neurotransmitter found free in the brain.



$$\underset{NH_2}{\overset{\gamma}{C}H_2}\overset{\beta}{C}H_2\overset{\alpha}{C}H_2—COOH$$

Amino acids which incorporate the anilino group are also of physiological importance. *p*-Aminobenzoic acid is required for the synthesis of the essential vitamin folic acid (chapter 27).



24.3 The Essential Amino Acids: Eat 'em or Else

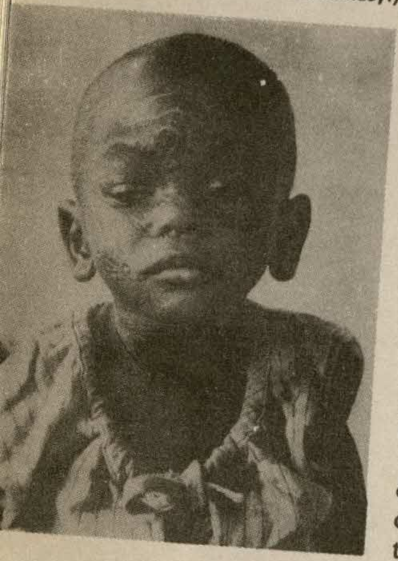


Figure 24.1 A lack of proteins and vitamins causes the deficiency disease known as kwashiorkor, which can be recognized by retarded growth, discoloration of the skin and hair, bloating, swollen belly, and mental apathy. (Courtesy of the World Health Organization, New York. Photo by Paul Almasy.)

The adult human body can synthesize all but eight of the amino acids needed for making proteins. Those eight (they are indicated in **table 24.1**) are called *essential amino acids*. They must be included in the diet. We eat proteins, break them down in our bodies to their constituent amino acids, and then use some of these amino acids to build other protein structures essential for health. Each of the essential amino acids is a *limiting reagent*. When the body runs out of one of them, synthesis of protein stops.

An *adequate protein* supplies all the essential amino acids in the quantities needed for growth and repair of body tissues. Most proteins from plant sources are deficient in one or more amino acids. Corn protein is lacking in lysine and tryptophan. People whose diet consists chiefly of corn may suffer from malnutrition even though the amount of calories supplied by the food is adequate. Protein from rice is short of lysine and threonine. Wheat protein is lacking in lysine. Even soy protein, probably the best nonanimal protein, is lacking in the essential amino acid methionine.

The breeding of high-lysine corn has met with some success. There is promise that other cereal grains can be bred to produce more and better protein. Missing amino acids can also be supplied as additives to inadequate proteins.

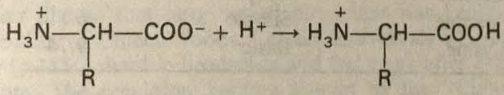
Most proteins from animal sources contain all the essential amino acids in adequate amounts. Lean meat, milk, fish, eggs, and cheese are adequate proteins. In fact, gelatin is about the only inadequate animal protein. It contains almost no tryptophan and has only small amounts of threonine, methionine, and isoleucine. A proper diet should consist of about 20% protein by weight. It must include all the essential amino acids in sufficient quantity.

Inadequate protein is already a problem in much of the world. A protein-deficiency disease called kwashiorkor (**figure 24.1**) is all too common in parts of Africa where corn is the major food. As population increases, animal protein will become scarcer in the developed countries.

Plants, such as grasses or grains, trap a small fraction of the energy of the sun that falls upon them. They use this energy to convert carbon dioxide, water, and mineral nutrients such as nitrates, phosphates, and sulfates into protein. Cattle eat the plant protein, digest it, and convert a small portion of it into animal protein. People eat this animal protein, digest it, and reassemble some of the amino acids into human protein. Some of the energy originally trapped by the green plants is lost at every step. If people ate the plant protein directly, one highly inefficient step would be skipped. Extreme vegetarianism is dangerous, however. One would have to eat a wide variety of plant materials to be sure of getting enough of all the essential amino acids. Even then, an all-vegetable diet is likely to be lacking in vitamin B_{12}, for this nutrient is not found in plants. Other nutrients scarce in all-plant diets include calcium, iron, riboflavin, and (for children not exposed to sunlight) vitamin D. A modified vegetarian diet which includes milk, eggs, cheese, and fish can provide excellent nutrition, with the total exclusion of red meat.

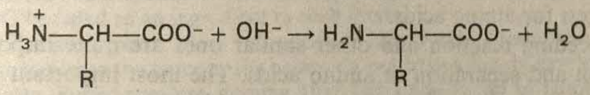
24.4 Reactions of Amino Acids: Pluses and Minuses

Amino acids can act either as acids or as bases. Indeed, they (and the proteins) act as buffers in living organisms. In the presence of added acid, the carboxylate group of the zwitterion captures protons.



$$\mathrm{H_3\overset{+}{N}{-}\underset{R}{CH}{-}COO^- + H^+ \longrightarrow H_3\overset{+}{N}{-}\underset{R}{CH}{-}COOH}$$

Note that the product is a positive ion. If base is added, protons are removed from the amino group of the zwitterion.

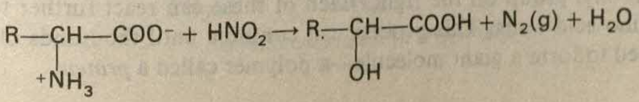


$$\mathrm{H_3\overset{+}{N}{-}\underset{R}{CH}{-}COO^- + OH^- \longrightarrow H_2N{-}\underset{R}{CH}{-}COO^- + H_2O}$$

In this case, a negative ion is formed. In both instances, the amino acid acts to maintain the pH of the system, that is, to tie up added acid and base.

At some intermediate pH value, an amino acid exists almost entirely as the zwitterion. That particular pH is called the *isoelectric point.* At the isoelectric point the positive and negative charges on an amino acid (or protein) just balance, and the molecule *as a whole* is electrically neutral. Note that the isoelectric point does *not* necessarily coincide with pH 7 (the value we ordinarily associate with neutrality). At its isoelectric point an amino acid (zwitterion) behaves very much like the salt of a weak acid and a weak base. As was noted in section 11.4, the solution of such a salt can be slightly acidic, slightly basic, or neutral. It depends on whether the acid or the base from which the salt was formed is stronger. Each amino acid has its own characteristic isoelectric point. The simple amino acids with un-ionizable side chains have isoelectric points ranging from pH 5.0 to pH 6.5. Basic amino acids (those in which the side chain incorporates a basic group) have isoelectric points at relatively high pH values. Acidic amino acids have isoelectric points at quite low pH values (**table 24.2**). By adjusting the pH of a solution, one can vary the net charge on an amino acid, thereby causing amino acids (or proteins) to migrate at different rates in an electric field. This process of separating mixtures of amino acids is called *electrophoresis*. It is one of the more important methods for separating proteins.

In addition to undergoing acid-base reactions, the amino acids also undergo the other characteristic reactions of carboxylic acids and amines. One of possible interest is that with nitrous acid. This reagent reacts with free amino groups, and nitrogen gas is formed.



$$\mathrm{R{-}\underset{^+NH_3}{CH}{-}COO^- + HNO_2 \longrightarrow R{-}\underset{OH}{CH}{-}COOH + N_2(g) + H_2O}$$

Table 24.2
Isoelectric points of representative amino acids

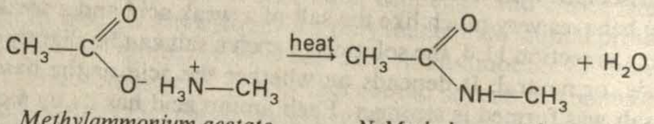
Amino Acid	*Class*	*pH*
Aspartic acid	Acidic	2.77
Glutamic acid	Acidic	3.22
Cysteine	Simple	5.02
Methionine	Simple	5.75
Tryptophan	Simple	5.89
Glycine	Simple	5.97
Alanine	Simple	6.11
Lysine	Basic	9.74

This reaction is the basis of the Van Slyke method for determining the number of free amino groups in a protein (chapter 19). The ninhydrin test (chapter 19) gives a purple color when amino acids are present and serves as a qualitative test for amino acids.

The preceding reaction and other similar ones are quite important in the detection and separation of amino acids. The most important reaction of all, though, is the polymerization reaction which forms peptides and proteins (sections 24.5 and 24.6).

24.5 Getting Yourself Together: The Peptide Bond

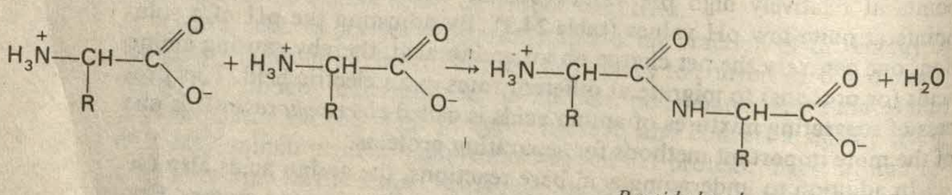
Proteins are polymers of amino acids. How are the monomer units held together? In chapter 19 we discussed the reaction of amines with carboxylic acid derivatives to form amides. If one heats the salt of an amine and a carboxylic acid, an amide is formed.



$$CH_3COO^- \; H_3\overset{+}{N}{-}CH_3 \xrightarrow{heat} CH_3CONH{-}CH_3 + H_2O$$

Methylammonium acetate *N-Methylacetamide*

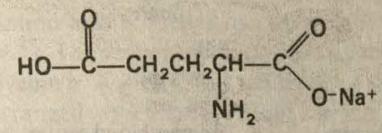
Similarly, the amino group on one amino acid molecule can react with the carboxyl group on another.



Peptide bond

The amide linkage (—CONH—) is called a *peptide bond* when it joins two amino acid units. Note that there is still a reactive amino group on the left and a carboxyl group on the right. Each of these can react further to join more amino acid units. This process can continue until thousands of units have joined to form a giant molecule—a polymer called a *protein*.

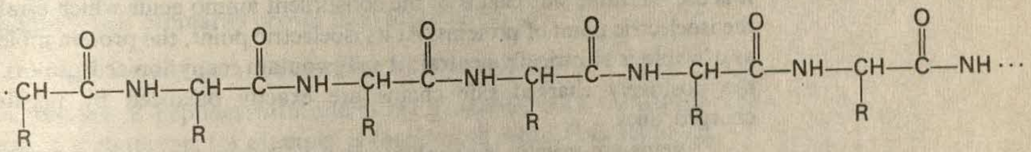
The sodium salt of glutamic acid, called monosodium glutamate (MSG), is a popular flavor-enhancing food additive.



MSG is used in many convenience foods. It is also heavily used in Chinese foods in restaurants in the United States. Although glutamates are found naturally in protein, there is evidence that excessive amounts are harmful. A peculiar disease that long baffled physicians was finally traced to the regular eating of Chinese foods. Certain individuals who are particularly sensitive to MSG develop headaches and feel weak after eating in Chinese restaurants. The condition became known as the "Chinese restaurant syndrome."

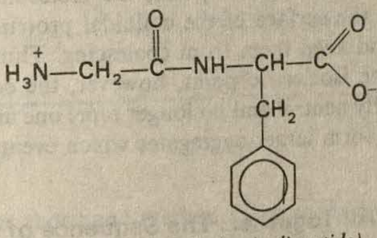
Those individuals who are susceptible to Chinese restaurant syndrome may have difficulty avoiding it. MSG is an ingredient of many prepared foods such as mayonnaise and salad dressings. There is no requirement that MSG be listed as an ingredient in such foods.

For many years, MSG was added to baby foods. Presumably, this was done to please the parents, for babies do not have a highly developed sense of taste. Public pressure, coming after MSG was found to numb portions of the brains of laboratory animals and to exert a possible teratogenic effect (i.e., to cause severe fetal defects), led to a voluntary withdrawal of MSG from baby foods by the processors.



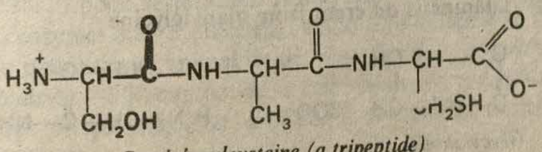
$$\cdots\underset{R}{\underset{|}{\mathrm{CH}}}-\overset{O}{\overset{\|}{\mathrm{C}}}-\mathrm{NH}-\underset{R}{\underset{|}{\mathrm{CH}}}-\overset{O}{\overset{\|}{\mathrm{C}}}-\mathrm{NH}-\underset{R}{\underset{|}{\mathrm{CH}}}-\overset{O}{\overset{\|}{\mathrm{C}}}-\mathrm{NH}-\underset{R}{\underset{|}{\mathrm{CH}}}-\overset{O}{\overset{\|}{\mathrm{C}}}-\mathrm{NH}-\underset{R}{\underset{|}{\mathrm{CH}}}-\overset{O}{\overset{\|}{\mathrm{C}}}-\mathrm{NH}-\underset{R}{\underset{|}{\mathrm{CH}}}-\overset{O}{\overset{\|}{\mathrm{C}}}-\mathrm{NH}\cdots$$

When only two amino acids are joined, the product is called a *dipeptide*.



Glycylphenylalanine (a dipeptide)

When three amino acids are combined, the substance is a *tripeptide*.



Serylalanylcysteine (a tripeptide)

Table 24.3
Isoelectric points of selected proteins

Protein	*Sourc*	*pH*
Silk fibroin	Silk	2.2
Casein	Cow's milk	4.6
Gelatin	Pig's feet	4.8
Serum albumin	Human blood serum	4.9
Albumin	Egg white	4.9
Lactoglobin	Cow's milk	5.2
Insulin	Cow's pancreas	5.3
Hemoglobin	Human red blood cells	6.7
Ribonuclease	Pancreas	9.5
Lysozyme	Egg white	10.7

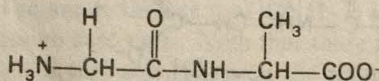
Note how these substances are named. Other combinations are named in a similar manner. Those with more than 10 amino acid units are often simply called *polypeptides*. When the molecular weight of a compound exceeds 10 000, it is called a protein. The distinction between polypeptides and proteins is an arbitrary one, and it is not always precisely applied. Nor need it be, for names are merely labels and do not change the properties of substances.

As with amino acids, every protein has a characteristic isoelectric point (**table 24.3**). In proteins, however, the alpha carboxyl and amino groups are tied up in the peptide bonds which hold the molecule together. Therefore, it is the ionizable side chains of the constituent amino acids which establish the isoelectric point of proteins. At its isoelectric point, the protein molecule as a whole is electrically neutral; it may contain many ionized groups, but the positively charged side chains are exactly balanced by negatively charged ones.

Proteins are usually *least* soluble at their isoelectric points. The size of many proteins places them in the category of colloids (section 9.10). At pH values other than the isoelectric point, the molecules carry a net charge. These charges on the surface of the colloidal proteins repel the other colloidal particles and keep them from coalescing. Thus, they form colloidal dispersions. At the isoelectric point, however, the colloidal protein molecules are electrically neutral and no longer repel one another. Therefore they come together to form larger aggregates which eventually precipitate from solution.

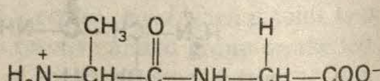
24.6 Getting It All Together: The Sequence of Amino Acids

For peptides and proteins to be physiologically active, it is not enough that they incorporate certain amounts of specific amino acids. The order or *sequence* in which the amino acids are connected is also of critical importance. Glycylalanine is different from alanylglycine.



$$H_3\overset{+}{N}-\overset{\overset{H}{|}}{C}H-\overset{\overset{O}{\|}}{C}-NH-\overset{\overset{CH_3}{|}}{C}H-COO^-$$

Glycylalanine



$$H_3\overset{+}{N}-\overset{\overset{CH_3}{|}}{C}H-\overset{\overset{O}{\|}}{C}-NH-\overset{\overset{H}{|}}{C}H-COO^-$$

Alanylglycine

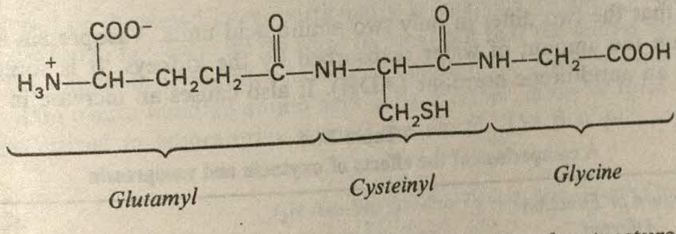
Although the difference seems minor, the two substances behave differently in the body.

When chemists describe peptides (and proteins), they find it much simpler to indicate the amino acid sequence by using the abbreviations for the amino acids (**table 24.1**). The sequence for glycylalanine is written Gly-Ala, and that for alanylglycine is Ala-Gly. It is understood from this shorthand that the peptide is arranged with the free amino group to the left and the free carboxyl group to the right.

As the length of a peptide chain increases, the possible sequential variations become almost infinite. And this potential for many different arrangements is exactly what one needs in a material which will make up such diverse things as hair and skin and eyeballs and toenails and a thousand different enzymes. Just as one can make millions of different words with our 26-letter English alphabet, one can make millions of different proteins with the 26 different amino acids. Just as one can write gibberish with the English alphabet, one can make nonfunctioning proteins by putting together the *wrong sequence* of amino acids. Yet while the correct sequence is ordinarily of utmost importance, it is not always absolutely required. Just as you can sometimes make sense of incorrectly spelled English words, a protein with a small percentage of "incorrect" amino acids may continue to function. It may not function as well, however, as a protein with the correct sequence. And sometimes a seemingly minor change can have a disastrous effect. Some people have hemoglobin with a single incorrect amino acid unit in about 300. That "minor" error is responsible for sickle cell anemia, an inherited condition which ordinarily proves fatal (chapter 28).

24.7 Think Small: Some Peptides of Interest

A number of peptides with interesting properties occur in nature. The tripeptide glutathione, for example, is found in all cells. Its structure is



$$\underbrace{\overset{+}{H_3N}-\overset{\overset{COO^-}{|}}{CH}-CH_2CH_2-\overset{\overset{O}{\|}}{C}}_{Glutamyl}-\underbrace{NH-\underset{\underset{CH_2SH}{|}}{CH}-\overset{\overset{O}{\|}}{C}}_{Cysteinyl}-\underbrace{NH-CH_2-COOH}_{Glycine}$$

We have not used our shorthand method for drawing the structure of this compound because of an interesting structural feature. The glutamic acid residue is connected to the rest of the peptide not through its alpha carboxyl group but through the carboxyl group of its side chain. Glutathione plays an important role in plant respiration. It may also function in animal cells to keep certain enzymes active. Since the amino acid cysteine as such is not present in large quantities in animal tissue, glutathione represents the most abundant sulfhydryl (—SH) compound in cells. Many enzymes also contain sulfhydryl groups (chapter 26). The oxidation of the groups to disulfides inactivates the enzymes.

$$2\ \text{Enzyme—SH} \rightarrow \text{enzyme—S—S—enzyme}$$

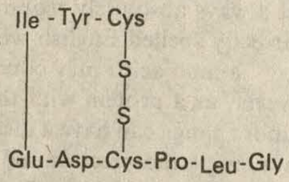
Active *Inactive*

Glutathione may function by reducing the enzymes back to free (and active) sulfhydryl compounds.

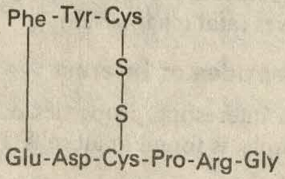
$$\text{Enzyme—S—S—enzyme} + 2\ \text{glutathione—SH} \rightarrow \text{glutathione—S—S—glutathione} + 2\ \text{enzyme—SH}$$

Many hormones (chapter 27) are peptides or proteins. Falling within the weight limits we have set for peptides are insulin and glucagon, pancreatic hormones which play important roles in the metabolism of carbohydrates (chapter 30).

Two smaller peptide hormones, vasopressin and oxytocin, are isolated from extracts of the posterior lobe of the pituitary gland. Both molecules are cyclic structures which incorporate a cystine unit with its disulfide bond.



Oxytocin



Vasopressin

Note that the two differ in only two amino acid units. Vasopressin acts to increase the amount of water reabsorbed by the kidneys. It is sometimes called an antidiuretic hormone (ADH). It also causes an increase in blood

Table 24.4
A comparison of the effects of oxytocin and vasopressin

Structure or Function Affected	*Vasopressin*	*Oxytocin*
Water diuresis	Inhibits	Has no effect on
Blood pressure	Elevates	Slightly lowers
Coronary arteries	Constricts	Slightly dilates
Intestinal contractions	Stimulates	Has questionable effect on
Uterine contractions*	**Stimulates**	Stimulates
Ejection of milk	**Slightly stimulates**	Stimulates

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*Response varies with species, as well as with the stage of the normal and the reproductive cycle.

pressure and has been used medically to combat the low blood pressure characteristic of postsurgical shock. Oxytocin governs smooth muscle contraction. It is involved in the uterine contractions which accompany childbirth and in the ejection of milk by lactating females. **Table 24.4** offers a comparison of the effects of vasopressin and oxytocin. Remember the great similarity in the structure of these compounds as you look at the table.

Bradykinin, a nonapeptide produced in the blood by the cleavage of larger protein molecules, has this sequence of amino acids.

Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg

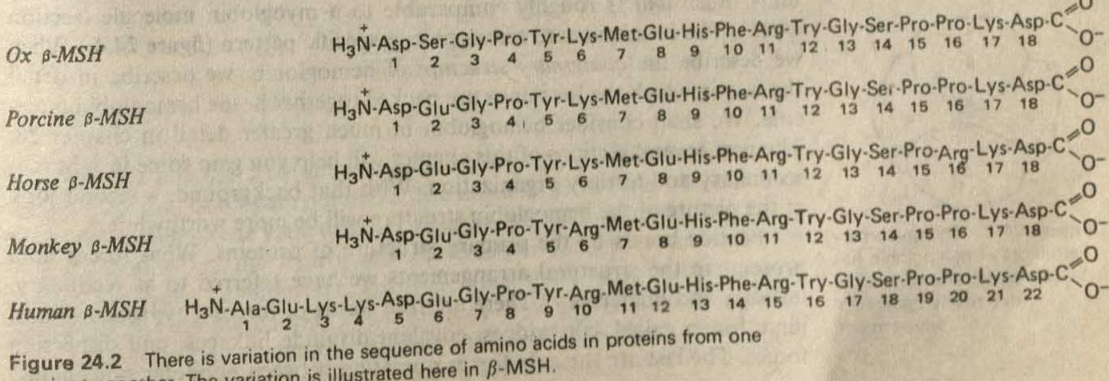
In terms of activity, bradykinin, a peptide, sounds almost like the prostaglandins, which are lipids (chapter 23). It is a very potent biochemical which causes a lowering of blood pressure, stimulation of smooth muscle tissue, an increase in capillary permeability, and pain. The reverse peptide has been synthesized.

Arg-Phe-Pro-Ser-Phe-Gly-Pro-Pro-Arg

It shows none of the activity of bradykinin.

As a final example we shall consider a hormone which regulates the coloring in animals, melanophore-stimulating hormone (MSH). Melanophores are cells which contain the pigments called melanins. MSH is involved in establishing protective coloration in animals. An injection of MSH will cause human skin to darken. There are two MSH groups, one designated alpha and one beta. The α-MSH from all species is identical. The β-MSH differs from one source to another (**figure 24.2**). Such variation from species to species is the rule rather than the exception.

There are many other physiologically important peptides. Quite a few of these will be discussed later, particularly in chapters 26 and 27. Before leaving the topic, however, we do want to point out that the amino acid sequences of hundreds of peptides have been determined. Some of these peptides contain over a hundred amino acid units. Further, many of these have been synthesized in laboratories around the world. The first polypeptide



Ox β-MSH $H_3\overset{+}{N}$-Asp-Ser-Gly-Pro-Tyr-Lys-Met-Glu-His-Phe-Arg-Try-Gly-Ser-Pro-Pro-Lys-Asp-$C(=O)O^-$ (1–18)

Porcine β-MSH $H_3\overset{+}{N}$-Asp-Glu-Gly-Pro-Tyr-Lys-Met-Glu-His-Phe-Arg-Try-Gly-Ser-Pro-Pro-Lys-Asp-$C(=O)O^-$ (1–18)

Horse β-MSH $H_3\overset{+}{N}$-Asp-Glu-Gly-Pro-Tyr-Lys-Met-Glu-His-Phe-Arg-Try-Gly-Ser-Pro-Arg-Lys-Asp-$C(=O)O^-$ (1–18)

Monkey β-MSH $H_3\overset{+}{N}$-Asp-Glu-Gly-Pro-Tyr-Arg-Met-Glu-His-Phe-Arg-Try-Gly-Ser-Pro-Pro-Lys-Asp-$C(=O)O^-$ (1–18)

Human β-MSH $H_3\overset{+}{N}$-Ala-Glu-Lys-Lys-Asp-Glu-Gly-Pro-Tyr-Arg-Met-Glu-His-Phe-Arg-Try-Gly-Ser-Pro-Pro-Lys-Asp-$C(=O)O^-$ (1–22)

Figure 24.2 There is variation in the sequence of amino acids in proteins from one species to another. The variation is illustrated here in β-MSH.

hormone synthesized was oxytocin, in 1953. Synthetic peptides have the same physiological properties as the corresponding natural ones. We won't go into the methods of sequencing and synthesis here. Suffice it to say that such methods, once laborious and time-consuming, have been largely automated.

24.8 Think Big: Structure and Classification of Proteins

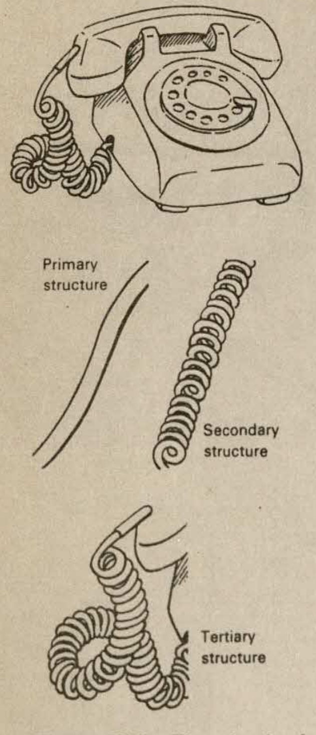


Figure 24.3 Three levels of structure of a telephone cord.

Proteins are big polypeptides, those with molecular weights of 10 000 or more. Some have molecular weights ranging into the millions. There are many kinds of proteins. Each has its own characteristic composition, amino acid sequence, and three-dimensional shape. The structure of proteins is generally discussed at four organizational levels. The *primary structure* of a protein molecule is its amino acid sequence. To specify the primary structure, one merely writes out the sequence of amino acids in the long-chain molecule. What "holds" the primary structure together are the peptide links between the amino acid units.

Molecules of proteins aren't just arranged at random as tangled threads. The chains are held together in unique configurations. The term *secondary structure* refers to the arrangement of chains about an axis. This arrangement may be a pleated sheet, as in silk (section 24.9), a helix, as in wool (section 24.10), or whatever. The term *tertiary structure* refers to the spatial relationships of amino acid units that are relatively far apart in the protein chain. In describing tertiary structure, we frequently will talk about how the molecule is *folded.* An example is the protein chain in myoglobin (section 24.12), which is folded into a compact, spherical shape.

We can relate these three levels of organization to a more familiar object. Think of the coiled cord on a telephone receiver. The cord starts out as a long, straight wire (**figure 24.3**). We'll call that the primary structure. The wire is coiled into a helical arrangement. That's its secondary structure. When the receiver is hung up, the coiled cord folds in a particular pattern. That would be its tertiary structure.

Some proteins contain more than one polypeptide chain; that is, a protein molecule can be an aggregate of subunits. Hemoglobin is the most familiar example. A single hemoglobin molecule contains four polypeptide units. *Each unit* is roughly comparable to a myoglobin molecule (section 24.12). The four units are arranged in a specific pattern (**figure 24.4**). When we describe the *quaternary structure* of hemoglobin, we describe in detail the way in which the four units are packed together in the hemoglobin molecule. We shall consider hemoglobin in much greater detail in chapter 28. The next several sections of this chapter will help you gain some insight into secondary and tertiary organization. With that background, a second look at the picture of the hemoglobin structure will be more worthwhile.

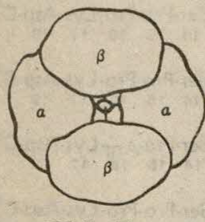
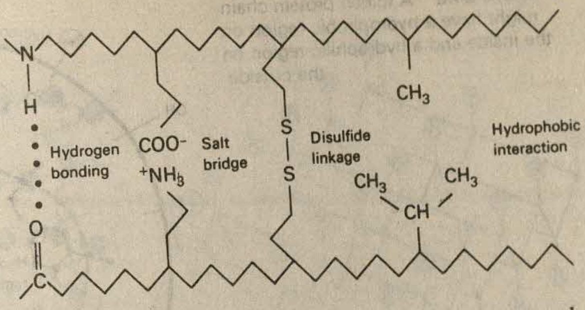


Figure 24.4 The quaternary structure of hemoglobin has the four coiled chains stacked in a nearly tetrahedral arrangement.

Peptide bonds fix the primary structure of proteins. What forces hold proteins in the structural arrangements we have referred to as secondary, tertiary, and quaternary? There are four kinds of forces—hydrogen bonds, ionic forces called salt bridges, covalent disulfide linkages, and dispersion forces. The last are the only forces operating between nonpolar side chains;

Figure 24.5 The forces holding protein chains together are of four types.

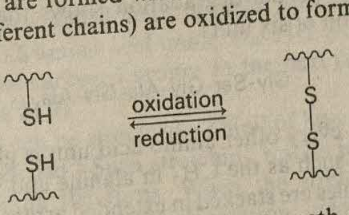


these are called hydrophobic interactions. The various forces are illustrated in **figure 24.5**.

A number of the amino acids have side chains which can and do participate in hydrogen bonding (the hydroxyl group of serine is one example). Nonetheless, the hydrogen bonds of greatest importance are those that involve an interaction between the atoms of one peptide bond and those of another. Thus, the carbonyl (C═O) oxygen of one peptide link may form a hydrogen bond to an amide (N—H) located some distance away on the same chain or located on an entirely different chain. The secondary structure of wool (section 24.10) illustrates the former situation; the secondary structure of silk (section 24.9) illustrates the latter. In both cases you will notice a pattern of such interactions. Because the peptide links are regularly spaced along the chain, there is a regular repetition of hydrogen bonds, both intramolecular (in wool) and intermolecular (in silk). Such patterns are a fairly common occurence.

As we saw in section 24.2, salt bridges occur when an amino acid with a basic side chain appears opposite one with an acidic side chain. Proton transfer results in opposite charges, which then attract one another. These interactions can occur between relatively distant groups which happen to come into contact because of some folding or coiling of a single chain. They also occur between chains.

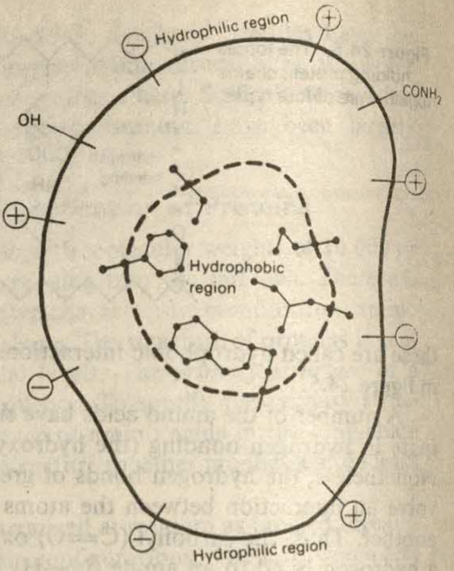
Disulfide linkages are formed when two cysteine units (whether on the same chain or two different chains) are oxidized to form a cystine unit.



The disulfide bond is a covalent bond. The strength of this bond is much greater than that of a hydrogen bond. The much larger number of hydrogen bonds does compensate somewhat for their individual weakness.

Still weaker are the hydrophobic interactions between nonpolar side chains. These can be important, however, when other types of interactions are missing or are minimized. The folding of some proteins (tertiary structure) sometimes brings nonpolar side chains inside the folded structure, in minimal contact with the aqueous solution surrounding the protein and in

Figure 24.6 A folded protein chain might have a hydrophobic region on the inside and a hydrophilic region on the outside.



close contact with one another (**figure 24.6**). Hydrophobic interactions become fairly significant in structures such as that of silk, in which a high proportion of amino acids in the protein have nonpolar side chains.

24.9 Silk: Purses, Petroleum, and Sows' Ears

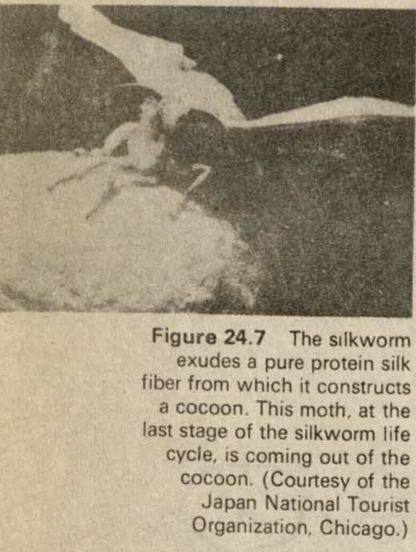


Figure 24.7 The silkworm exudes a pure protein silk fiber from which it constructs a cocoon. This moth, at the last stage of the silkworm life cycle, is coming out of the cocoon. (Courtesy of the Japan National Tourist Organization, Chicago.)

Silk is a fine, soft, shiny fiber produced by the silkworm (**figure 24.7**) as it spins its cocoon. It was once widely used in clothing for the well-to-do. The expressions "silk hat" and "silk stocking district" are relics of another age, for silk has been largely replaced by synthetics such as nylon (chapter 21).

Silk consists of *fibroin*, a fibrous protein. The polypeptide chains exist in an extended zigzag arrangement (**figure 24.8**). Unlike most proteins, silk is composed primarily of just three amino acids, glycine (45%), alanine (30%), and serine (12%), with the remaining 13% being made up of various other amino acids. Indeed, partial degradation shows that much of each chain consists of a repetition of six units.

··· Gly-Ser-Gly-Ala-Gly-Ala ···

In this arrangement, every other amino acid unit is glycine. Most of the remaining side chains, such as the CH_3 in alanine and the CH_2OH in serine, are small. The molecules are stacked in extended arrays, with hydrogen bonds holding adjacent chains together. The appearance of this arrangement (**figure 24.8**) has led to its designation as the *pleated sheet conformation*. Silk fibers have these hydrogen-bonded layers arranged one over the other.

The properties of silk—strength, flexibility, and resistance to stretching—are a consequence of its structure. To break the fibers would involve rupturing thousands of hydrogen bonds or breaking covalent bonds. The interaction of small side chains allows for great flexibility, and since the chains are already fully extended, the fibers cannot be stretched easily.

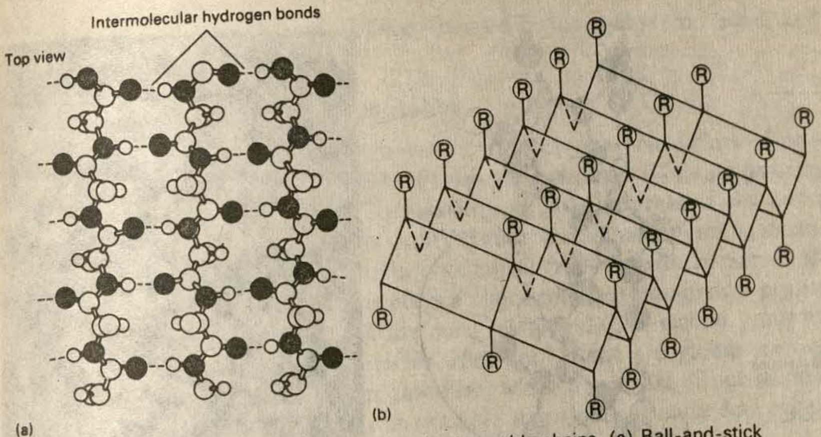


Figure 24.8 Pleated sheet conformation of polypeptide chains. (a) Ball-and-stick model. (b) Schematic drawing emphasizing the pleats. (Reprinted with permission from Gutsche, C. David, and Pasto, Daniel J., *Fundamentals of Organic Chemistry*, Englewood Cliffs, N.J.: Prentice-Hall, 1975. Copyright © 1975 by Prentice-Hall, Inc.)

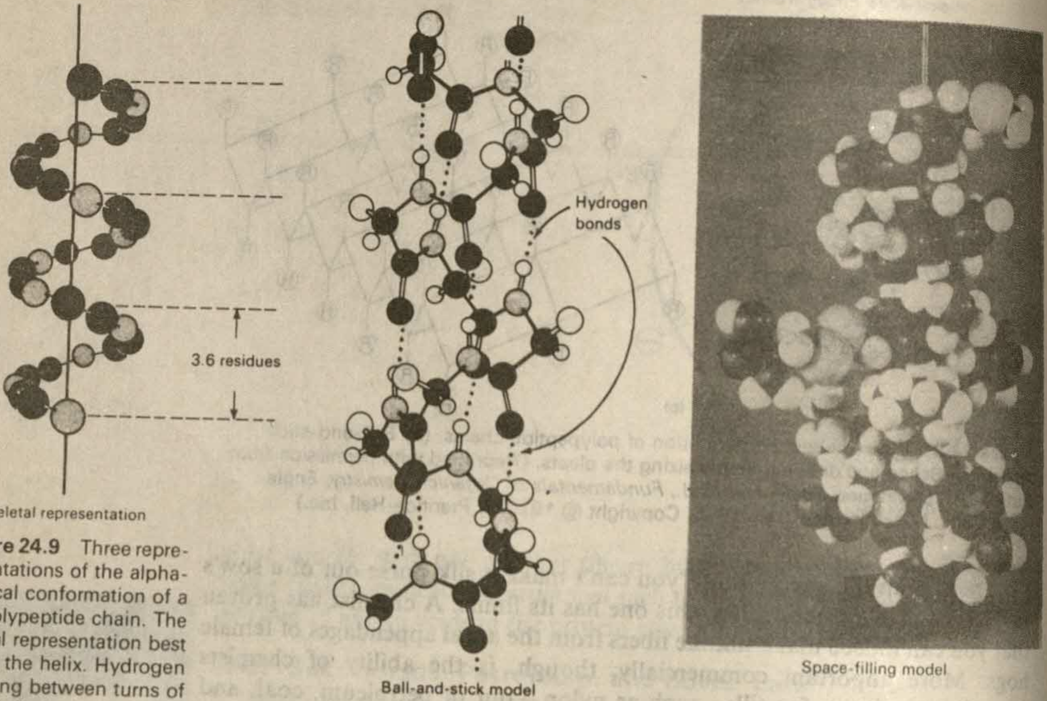
There is an old saying that "you can't make a silk purse out of a sow's ear." Like many other clichés, this one has its limits. A chemist has proven that you can indeed make silklike fibers from the aural appendages of female hogs. More important commercially, though, is the ability of chemists to make substitutes for silk—such as nylon—out of petroleum, coal, and air.

24.10 Wool: From Little Lambs to Linus Pauling

Wool is another natural protein material, but its composition and properties are quite different from those of silk. Wool has a greater variety of amino acids than silk, including many with large side chains. The structure of proteins such as wool, hair, and muscle was first determined by Linus Pauling and coworkers in 1950. Pauling showed that the amino acid units were arranged in a right-handed helix, or *alpha helix* (**figure 24.9**). Each turn of the helix requires 3.6 amino acid units. The NH groups in one turn form hydrogen bonds to the carbonyl groups in the next (the dotted lines in the center model of **figure 24.9**).

Unlike silk, wool can be stretched. (Think of how the coiled wire on the telephone can be stretched.) Such stretching results in an elongation of the hydrogen bonds joining the turns. When the stretching is discontinued, the helix will return to its original configuration, unless, of course, you have radically disrupted the structure by treating the wool with very hot water (section 24.13).

Hair, horn, nails, and muscles also have the alpha-helical structure. This helix extends along the axis of the fiber. Adjacent helices are not precisely parallel but are wound about one another like the strands of a rope. These ropes, called protofibrils, may have three or seven alpha helices as strands. Horns, nails, and claws have less flexibility than wool and hair, due to more extensive cross-linking by disulfide bridges.



Skeletal representation

Ball-and-stick model

Space-filling model

Figure 24.9 Three representations of the alpha-helical conformation of a polypeptide chain. The skeletal representation best shows the helix. Hydrogen bonding between turns of the helix is shown in the ball-and-stick model. The space-filling model shows the actual shape of a short segment of the chain. (Skeletal representation and ball-and-stick model reprinted with permission from Gutsche, C. David, and Pasto, Daniel J., *Fundamentals of Organic Chemistry*, Englewood Cliffs, N.J.: Prentice-Hall, 1975. Copyright © 1975 by Prentice-Hall, Inc. Space-filling model courtesy of Science-Related Materials, Inc., Janesville, Wis.)

24.11 Collagen: The Protein of Connective Tissues

The principal protein of connective tissues is *collagen*. As much as 60% of all mammalian protein is of this type. Most of the organic portion of skin, bones, tendons, and teeth is collagen. It also occurs in most other parts of the body as fibrous inclusions. Like the other fibrous proteins, collagen is not readily digestible. Treatment with boiling water converts collagen to *gelatin*. Gelatin is not only water soluble but digestible. The cooking of meat converts part of the tough connective tissue to gelatin, making the meat more tender.

In composition, collagen is about 33% glycine, with another 20% to 25% consisting of the heterocyclic compounds proline and hydroxyproline (**table 24.1**). Collagen also contains acidic and basic amino acids. It does not contain enough of the essential amino acids; the gelatin derived from it is a poor-quality protein.

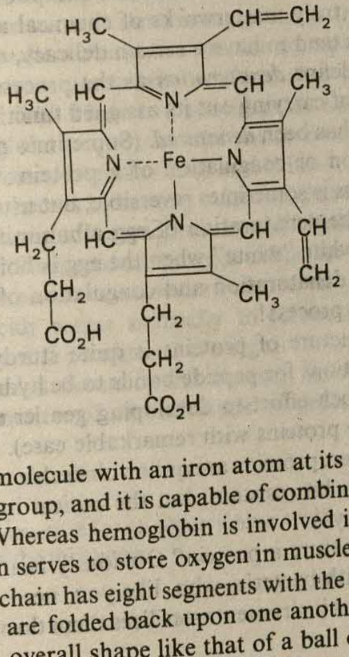
Structurally, collagen consists of three protein chains, each wound about its own axis in a left-handed helix (**figure 24.10**). Unlike wool, collagen does not have hydrogen bonding between coils. Indeed, its structure is much more open than that of the tightly coiled alpha helix. Hydrogen bonds between chains do hold the three chains of collagen together. Collagen chains are also somewhat cross-linked by covalent bonds. As an animal grows older, the extent of cross-linking increases, and the meat gets tougher.

Collagen is of considerable commercial importance. The process of tanning increases the degree of cross-linking, converting skin to leather. The soluble gelatin derived from collagen is used in food, film emulsions, and glue and in many other ways.

24.12 Globs of Protein: Myoglobin

Fibrous proteins, insoluble in water, make up one broad class of proteins. The other major class consists of the *globular proteins*. Globular proteins are soluble in aqueous media. The mixtures of globular proteins and water are actually colloidal dispersions rather than true solutions. Familiar examples are the *albumins*. Egg albumin is obtained from egg whites. Serum albumin is present in blood, and it plays a major role in maintaining a proper balance of osmotic pressures in the body (chapter 28). A second group of globular proteins are called *globulins*. Hemoglobin and myoglobin are two examples. Another is the serum globulins, which are a part of our defense against disease. We will discuss one example, myoglobin, in some detail since its characteristics are rather typical.

Myoglobin molecules consist of a single chain of 153 amino acid residues. Myoglobin also contains a *heme* unit. The structure of heme, also found in hemoglobin, is



It is a relatively flat molecule with an iron atom at its center. The heme unit is called a *prosthetic* group, and it is capable of combining with oxygen under proper conditions. Whereas hemoglobin is involved in oxygen transport in the blood, myoglobin serves to store oxygen in muscle tissue.

The polypeptide chain has eight segments with the alpha-helical structure (**figure 24.11**). These are folded back upon one another in such a way as to give the molecule an overall shape like that of a ball or globe. The shape of the final molecule includes a hole which nicely accommodates the heme unit. The tertiary structure also brings two amino acid side chains into position to anchor the heme unit to the protein portion of the myoglobin molecule.

There are many other proteins of vital importance. We will encounter several more, including the all-important enzymes, in subsequent chapters.

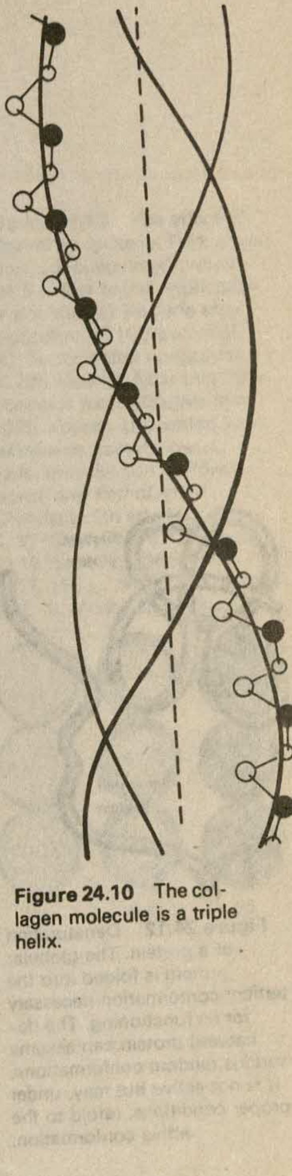
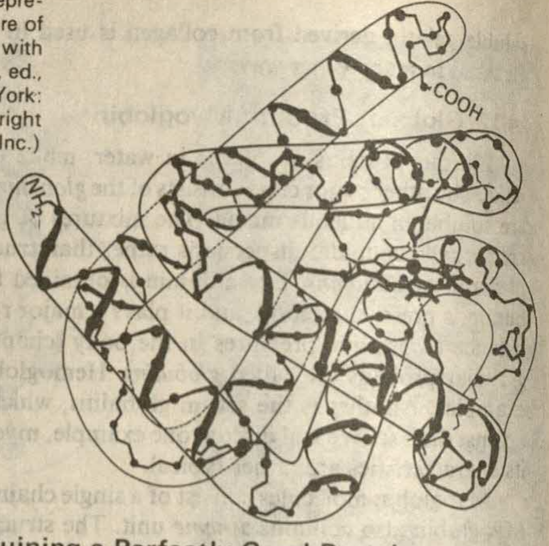


Figure 24.10 The collagen molecule is a triple helix.

Figure 24.11 A skeletal representation of the tertiary structure of myoglobin. (Reprinted with permission from Neurath, H., ed., *The Proteins*, vol. 2, New York: Academic Press, 1964. Copyright © 1964 by Academic Press, Inc.)



24.13 Denaturation: Ruining a Perfectly Good Protein

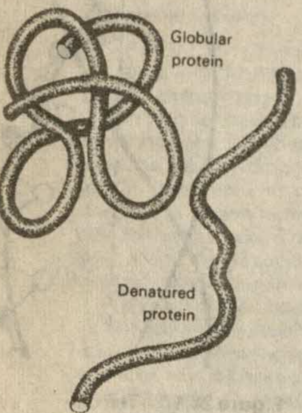


Figure 24.12 Denaturation of a protein. The globular protein is folded into the tertiary conformation necessary for its functioning. The denatured protein can assume various random conformations. It is not active but may, under proper conditions, refold to the active conformation.

In many ways, proteins are remarkable compounds. Their highly organized structures are truly masterworks of chemical architecture. But highly organized structures tend to have a certain delicacy, and this is true of many proteins. We shall define *denaturation* as the process in which a protein is rendered incapable of carrying out its assigned function. If the protein can't do its job, we say it has been *denatured*. (Sometimes denaturation is equated with the precipitation or coagulation of a protein. Our definition is a bit broader.) The process is sometimes reversible, but usually it is not. You have certainly observed the denaturation of egg albumin. The clear egg "white" turns to an opaque white "white" when the egg is boiled or fried. What you are observing is the denaturation and coagulation of the albumin. No one has yet reversed that process!

The primary structure of proteins is quite sturdy. In general, it takes fairly vigorous conditions for peptide bonds to be hydrolyzed (though chemists have devoted much effort to developing gentler methods and enzymes manage to hydrolyze proteins with remarkable ease). At the secondary and tertiary levels, however, proteins are quite vulnerable to attack (**figure 24.12**). Disulfide bonds are a bit resistant, but the critical hydrogen bonds can be disrupted in many ways.

How can you denature a protein? Obviously heat is one way. It works with eggs and also with bacteria, who, like you, need active protein to live. Autoclaving of surgical instruments sterilizes them through the action of heat on bacterial protein.

Other forms of energy can be used; ultraviolet light, for example, will denature protein and is occasionally used for sterilization.

Chemicals can be used. Ethyl alcohol will badly disrupt the hydrogen bonds of proteins. It sterilizes the skin (by killing bacteria present) when injections are to be given. A 70% aqueous solution is used rather than the more commonly available 95% because the higher concentration is so effective at coagulating protein that it forms a surface "crust" which prevents the interior of the bacteria from being attacked. There is also a group of acidic compounds referred to as alkaloidal reagents (they react with alkaloids) which will react with proteins. The reagents disrupt salt bridges and hydrogen bonds and cause precipitation of the protein. One, tannic acid, is sometimes applied to severe burns. The precipitated protein forms a crust over the wounds and thus slows the loss of body fluids.

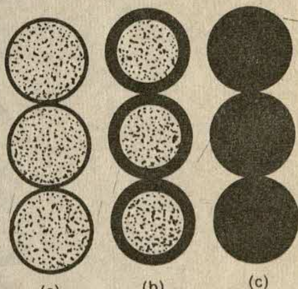
Heavy metals (lead and mercury, for example) denature proteins and bring about their coagulation, probably by interacting with sulfhydryl groups or ionizable side chains. That can be very bad when the protein is an essential enzyme (chapter 26). Mercury poisoning and lead poisoning are debilitating diseases that are potentially fatal. There is a positive side, however. An antidote can take advantage of the same phenomenon. A person who had ingested mercury could be fed raw eggs immediately. The mercury would then react with egg protein in the stomach rather than with other, more essential proteins. This treatment would require that the stomach contents be pumped out or vomited to prevent the ultimate digestion of the egg protein and the consequent release in the body of mercury ions. Quite clearly, the technique works only for acute poisonings and not for the far more common chronic mercury poisoning (chapter 26).

There are many other ways of denaturing proteins that we have not discussed (introduction of radical changes in pH, for example). The point should be clear, however. The very complexity which makes proteins so versatile also makes them vulnerable. There is a considerable range of vulnerability. The delicately folded globular proteins are much more readily denatured than are the tough, fibrous proteins of hair and skin.

On the other hand, there is increasing evidence that an unfolded protein, given the proper conditions and enough time, will refold and may again exhibit biological activity. Such evidence suggests that, for these molecules, the primary structure determines the secondary and tertiary structures. A given sequence of amino acids seems naturally to adopt its particular three-dimensional arrangement if conditions are right.

We have emphasized structure in this chapter. In later chapters we will concentrate on the function of several kinds of proteins, particularly the enzymes.

Figure 24.13 The effect of alcohol on bacteria. Dark areas represent coagulated protein. (a) Bacteria before application of alcohol. (b) Bacteria after application of 100% alcohol. (c) Bacteria after application of 70% alcohol. Note that 70% alcohol is more effective than 100% alcohol. (Reprinted with permission from Arnow, L. Earle, *Introduction to Physiological and Pathological Chemistry*, 9th ed., St. Louis: C. V. Mosby, 1976. Copyright © 1976, 1972, 1966, 1961, 1957, 1953, 1949, 1943, 1939 by C. V. Mosby Company.)



Problems

1. What is the general structure for an alpha amino acid?
2. Write a structure for the following.
    a. glycine
    b. alanine
    c. phenylalanine
    d. glycylalanine
    e. alanylglycine
    f. phenylalanylglycylalanine
    g. an amino acid with an acidic side chain
    h. an amino acid with a basic side chain
    i. cysteine
    j. cystine
    k. the anion formed when glycine reacts with base

    l. the cation formed when alanine reacts with acid
    m. the products obtained from the complete hydrolysis of the peptide phenylalanylglycylalanine.

3. What is the difference between polypeptides and proteins?
4. Define, describe, or illustrate each of the following.
    a. peptide bond
    b. sequence of amino acids
    c. essential amino acid
    d. disulfide linkage
    e. salt bridge
    f. hydrophobic interaction
    g. primary structure
    h. secondary structure
    i. tertiary structure
    j. quaternary structure
    k. zwitterion
    l. isoelectric point
    m. a complete (adequate) protein
    n. globular protein
    o. fibrous protein
5. Explain why a diet high in meat products makes less efficient use of the energy originally captured by plants through photosynthesis.
6. In general, what are the potential problems associated with a strict vegetarian diet?
7. Describe the structure of silk and explain how its properties reflect its structure. What name is given to the secondary structure of silk?
8. Write an equation to show the hydrolysis of alanylglycine. (Recall the hydrolysis of an amide, discussed in chapter 18.)
9. Write an equation to show the conversion of cysteine to cystine. (Recall the oxidation of a thiol to a disulfide, described in chapter 20.)
10. Describe the structure of wool and relate this to wool's elasticity. What name is given to the secondary structure of wool protein?
11. Describe the structure of collagen. Why is a steak from an old cow so tough?
12. How does the structure of myoglobin differ from that of wool or silk?
13. Using the formula given in section 24.7 (p. 504), write the shorthand structure of the product which would result from the reduction of the disulfide bond in oxytocin. Do you think the product would show the same biological activity as oxytocin?
14. What do we mean when we say that hemoglobin shows species variation?
15. Describe some ways of denaturing a protein. Is denaturation reversible? What level(s) of structure is (are) ordinarily disrupted in denaturation?

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chapter 25

Nucleic Acids

In spy stories of fact and fiction, a key event is often the cracking of an enemy's code. It was near the middle of this century that one of history's most thrilling adventures in code breaking took place. It involved many scientists from several nations, but the crucial breakthrough in the deciphering of the code of life itself was accomplished by James Watson and Francis Crick. They discovered the mechanism whereby nucleic acid molecules transmit the patterns of life from one generation to the next. In doing so, they helped start a new era of biological investigation.

The nucleic acids also control the synthesis of proteins. Each organism produces its own set of enzymes to mediate the chemical reactions that make it what it is.

The story is far from complete. We have just learned the alphabet and have put together a few simple words. Much more research will have to be done before we can formulate more than a simple outline of the story of life. Yet a beginning has been made. What we have learned of the code of life we have already used to improve human health. Even more significant applications—the repair of defective genes, the design of precise molecular medicine, and much more—will be developed in the future.

25.1 The Building Blocks of Nucleoproteins

Nucleoproteins are found in every living cell. They are exceedingly complex, as might be expected from the role they play: they are the information and control centers of the cell. More about that later in the chapter. Let's look first at what nucleoproteins are made of. One way to find out is to take them apart.

Working carefully, chemists can separate nucleoproteins into a nucleic acid portion and a protein portion.

$$\text{Nucleoprotein} \longrightarrow \text{nucleic acid} + \text{protein}$$

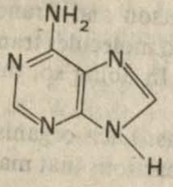
The protein is highly basic. Hydrolysis reveals that it contains many units of the amino acids lysine and arginine.

$$\text{Protein} \xrightarrow{H_2O} \text{lysine} + \text{arginine} + \text{other amino acids}$$

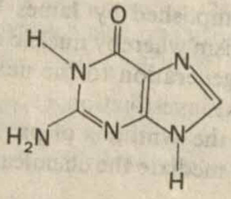
The nucleic acids can also be hydrolyzed. Controlled hydrolysis gives units called *nucleotides*. These can be further hydrolyzed to phosphoric acid and compounds called *nucleosides*. Nucleosides can be hydrolyzed to the ultimate molecular constituents which are purine and pyrimidine bases (chapter 19) and a pentose sugar (chapter 22).

$$\text{Nucleic acids} \xrightarrow{H_2O} \text{nucleotides} \xrightarrow{H_2O} \left\{ \begin{array}{c} \text{nucleosides} \\ + \\ H_3PO_4 \end{array} \right. \xrightarrow{H_2O} \left\{ \begin{array}{c} \text{two purine bases} \\ + \\ \text{two pyrimidine bases} \\ + \\ \text{a pentose sugar} \end{array} \right.$$

There are actually two kinds of nucleic acids. Each is a gigantic polymer with nucleotides as the repeating units. Deoxyribonucleic acid (DNA) occurs in the cell nucleus. Ribonucleic acid (RNA) is found in all parts of the cell. The two nucleic acids differ only slightly in composition. Complete hydrolysis of DNA ultimately gives two purine bases, adenine and guanine, and two pyrimidine bases, cytosine and thymine.

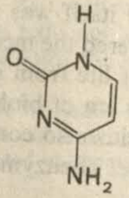


Adenine

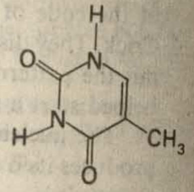


Guanine

Purine bases



Cytosine



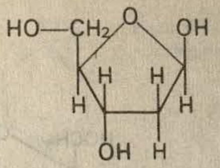
Thymine

Pyrimidine bases

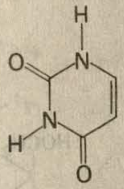
Also obtained from DNA are phosphoric acid and the simple sugar 2-deoxyribose.

Table 25.1
Ultimate hydrolysis products of DNA and RNA

	DNA	*RNA*
Purine bases	Adenine Guanine	Adenine Guanine
Pyrimidine bases	Cytosine Thymine	Cytosine Uracil
Pentose sugar	2-Deoxyribose	Ribose
Inorganic acid	Phosphoric acid	Phosphoric acid

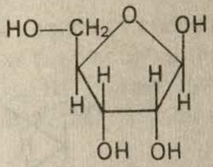


Ribonucleic acid (RNA) differs only in that one of the pyrimidine bases, thymine, is replaced by another, uracil,



Uracil

and the sugar, deoxyribose, is replaced by ribose.



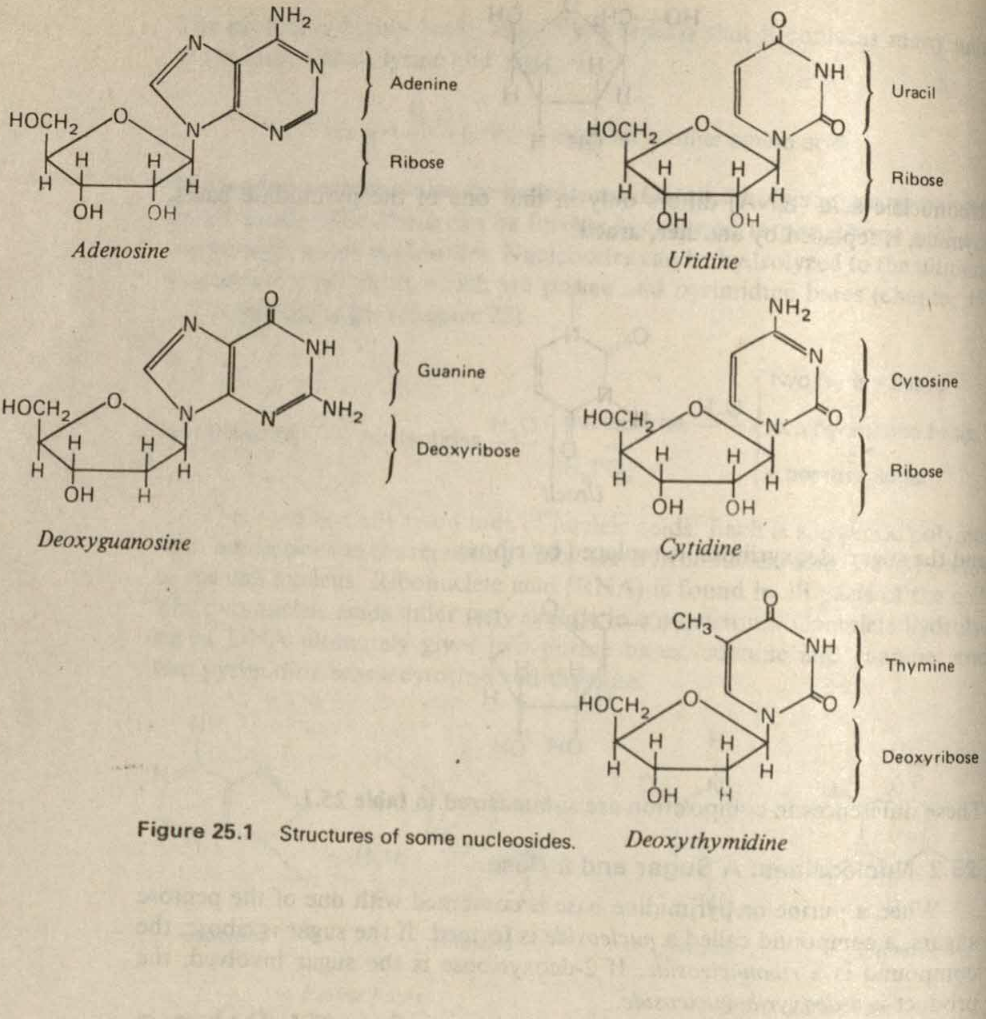
These differences in composition are summarized in **table 25.1.**

25.2 Nucleosides: A Sugar and a Base

When a purine or pyrimidine base is combined with one of the pentose sugars, a compound called a *nucleoside* is formed. If the sugar is ribose, the compound is a *ribonucleoside*. If 2-deoxyribose is the sugar involved, the product is a *deoxyribonucleoside*.

Several representative nucleosides are shown in **figure 25.1.** The bases in these molecules are attached at the first carbon of the pentose unit, replacing a hydroxyl group that ordinarily appears there. Note that *adenosine* is derived from adenine and ribose. Uridine is similarly derived from uracil and ribose. Deoxythymidine is made up of the base thymine and the pentose 2-deoxyribose. Since there are 5 bases and 2 sugars, 10 nucleosides are possible. Half of these would be deoxynucleosides and half would be ribonucleosides. Only 8 of the 10 are obtained by hydrolysis of natural nucleic acids, though. Thymine would not be found combined with ribose, nor would uracil be found with 2-deoxyribose. Those combinations just aren't found in either RNA or DNA.

Several nucleoside derivatives have been used in medicine. One, puromycin (**figure 25.2**) is derived from adenosine. It is an antibiotic. First obtained from cultures of the fungus *Streptomyces alboniger*, puromycin is effective against protozoa and has shown some antitumor activity.



Adenosine

Uridine

Deoxyguanosine

Cytidine

Figure 25.1 Structures of some nucleosides.

Deoxythymidine

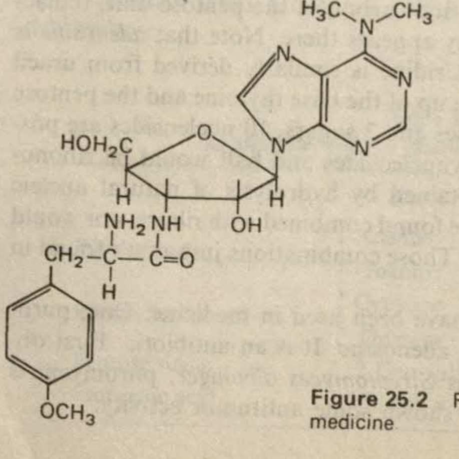
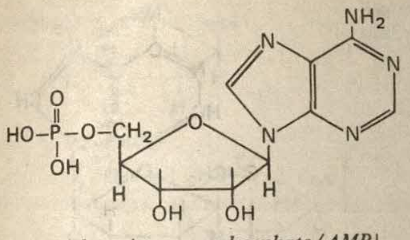
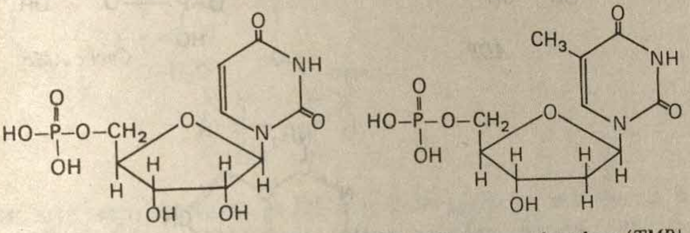


Figure 25.2 Puromycin, a nucleoside derivative used in medicine



Adenosine monophosphate (AMP)



Uridine monophosphate (UMP) *Thymidine monophosphate (TMP)*

Figure 25.3 Structures of three important nucleotides.

25.3 Nucleotides: A Sugar, a Base, and a Phosphate

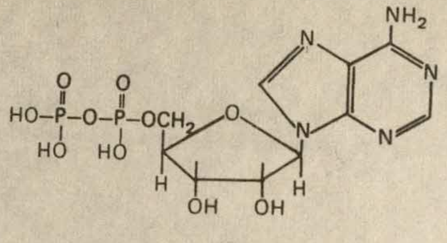
Nucleotides are phosphate esters of nucleosides. A hydroxyl group on the pentose molecule serves as the alcohol in the esterification process. The primary alcohol group (—CH_2OH) is generally the one involved. (Compare the nucleoside adenosine, in **figure 25.1**, with the nucleotide adenosine monophosphate, in **figure 25.3**.)

The nucleotides are named in two ways. One involves dropping the ending from the name of the corresponding nucleoside (either *-ine* or *-osine*) and adding the ending *-ylic acid*. Thus, the nucleoside uridine, upon esterification with phosphoric acid, becomes uridylic acid. Similarly, guanosine becomes guanylic acid. The other system, simpler and more frequently used, involves using the nucleoside name as is and adding the word *monophosphate*. Thus, adenosine, upon esterification, becomes adenosine monophosphate, often abbreviated AMP. The prefix *deoxy-* indicates that the sugar involved is deoxyribose rather than ribose. These naming systems are summarized in **table 25.2**.

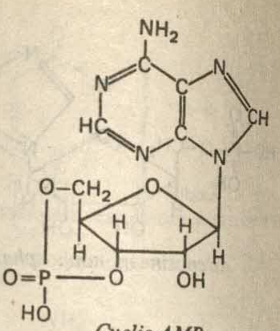
Table 25.2
Naming the nucleotides

Base	*Nucleoside*	*Nucleotide* *As an Acid*	*As a Monophosphate*	*Abbreviation*
Adenine	Adenosine	Adenylic acid	Adenosine monophosphate	AMP
Guanine	Guanosine	Guanylic acid	Guanosine monophosphate	GMP
Cytosine	Cytidine	Cytidylic acid	Cytidine monophosphate	CMP
Thymine	Thymidine*	Thymidylic acid*	Thymidine monophosphate*	TMP*
Uracil	Uridine	Uridylic acid	Uridine monophosphate	UMP

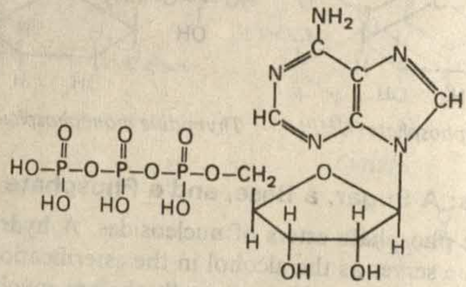
*The prefix *deoxy-* generally indicates that the sugar 2-deoxyribose is present rather than ribose. Because thymine occurs *only* with deoxyribose, the prefix is not used for its derivatives.



ADP



Cyclic AMP



ATP

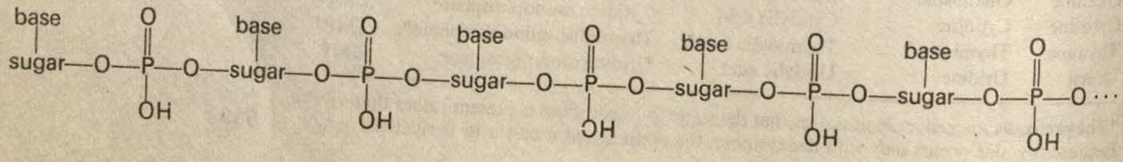
Figure 25.4 Structures of three important nucleotide derivatives.

The structures of three representative nucleotides are given in **figure 25.3.** Nucleotides are the monomers from which DNA and RNA are synthesized. In addition, the nucleotides and some of their derivatives carry out a variety of other functions in the cell. Adenosine diphosphate (ADP) and adenosine triphosphate (ATP) are involved in many metabolic and biosynthetic processes. We shall encounter them often in subsequent chapters. A cyclic phosphate ester of adenosine, called cyclic AMP, serves as a mediator in many cellular processes, including the synthesis of proteins and steroids and the metabolism of carbohydrates and fats. Structures of these nucleotide derivatives are shown in **figure 25.4.**

25.4 The Base Sequence: Primary Structure of Nucleic Acids

The nucleic acids are polymers of nucleotides. The backbone of the polymer is a polyester chain. This backbone involves the phosphoric acid and the pentose sugar portions of the nucleotides. The connection between one nucleotide unit and the next is made when a phosphate hydroxyl group in one unit reacts with a sugar hydroxyl on the next (**figure 25.5**).

A base is attached to each sugar unit. The polymer can be represented schematically by



$$\overset{\text{base}}{\overset{|}{\text{sugar}}}\text{—O—}\underset{\text{OH}}{\underset{|}{\overset{\text{O}}{\overset{\|}{\text{P}}}}}\text{—O—}\overset{\text{base}}{\overset{|}{\text{sugar}}}\text{—O—}\underset{\text{OH}}{\underset{|}{\overset{\text{O}}{\overset{\|}{\text{P}}}}}\text{—O—}\overset{\text{base}}{\overset{|}{\text{sugar}}}\text{—O—}\underset{\text{OH}}{\underset{|}{\overset{\text{O}}{\overset{\|}{\text{P}}}}}\text{—O—}\overset{\text{base}}{\overset{|}{\text{sugar}}}\text{—O—}\underset{\text{OH}}{\underset{|}{\overset{\text{O}}{\overset{\|}{\text{P}}}}}\text{—O—}\overset{\text{base}}{\overset{|}{\text{sugar}}}\text{—O—}\underset{\text{OH}}{\underset{|}{\overset{\text{O}}{\overset{\|}{\text{P}}}}}\text{—O}\cdots$$

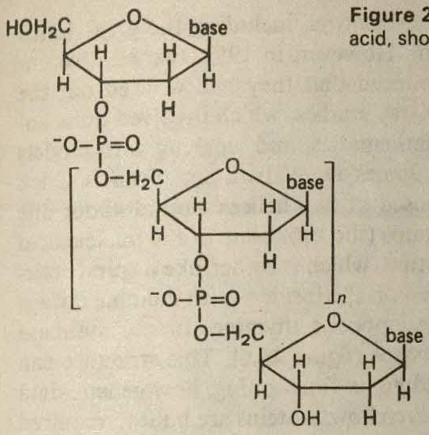


Figure 25.5 The polymeric backbone of a nucleic acid, shown here for deoxyribonucleic acid.

As we have seen, the sugar in DNA is 2-deoxyribose, and that in RNA is ribose. The bases in DNA are adenine, guanine, cytosine, and thymine. Those in RNA are adenine, guanine, cytosine, and uracil. Note the one ionizable hydrogen on each phosphate unit. That is what makes these compounds nucleic *acids*. However, in solution or combined with basic proteins as nucleoproteins, the acid may be ionized (**figure 25.5**).

Nucleic acids resemble proteins in one respect: to completely specify the primary structure of a nucleic acid, one must specify the *sequence* of bases. Unlike the proteins, which have 26 different amino acids, there are only 4 different bases in a nucleic acid. However, the molecular weight of nucleic acids is much greater than that of proteins, ranging into the billions for mammalian DNA. This makes the problem of sequencing much more difficult for nucleic acids than for proteins. Some RNA molecules are simpler, and the base sequences of a few have been determined. For example, the primary structure of the nucleic acid called alanine transfer RNA, a molecule with 77 nucleotide units, has been determined. The work, done by Robert W. Holley and coworkers at Cornell University, took 7 years. Holley was rewarded with a share of the Nobel Prize in 1968 for his part in the project.

The determination of the base sequence in other RNAs has been accomplished in recent years. The primary structure of DNA, with molecules thousands of times as long, is much more difficult to work out. Research in this area is now under way, however.

25.5 The Secondary Structure of Nucleic Acids: Base Pairing and the Double Helix

The shape of the giant DNA molecules was long a mystery. Early studies revealed no more than the fact that the structure exhibited a periodic pattern. A real breakthrough occurred in 1950, when Erwin Chargoff, of Columbia University, showed that the molar amount of adenine (A) in DNA was always equal to that of thymine (T). Similarly, the molar amount of guanine (G) was the same as that of cytosine (C). The bases must be paired, A to T and G to C. But how? The race was on, with an almost certain Nobel

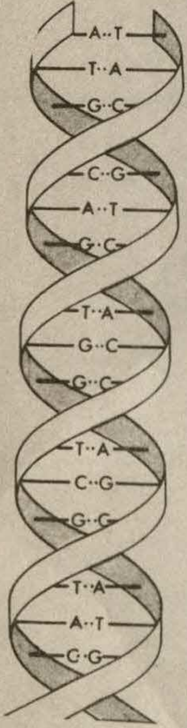


Figure 25.6 The DNA double helix as portrayed by Watson and Crick.

Prize for the winner. Many illustrious scientists, including the great Linus Pauling, were working on the problem. However, in 1953, two relative unknowns in the world of science announced that they had worked out the structure of DNA. Using data from X-ray studies, which involved quite sophisticated chemistry, physics, and mathematics, and working with models not unlike a child's construction set, James D. Watson and Francis Crick determined that DNA must be composed of two helices wound about one another. The phosphate and sugar groups (the backbone of the nucleic acid polymer) form the outside of the structure, which is rather like a spiral staircase. The heterocyclic amines are paired on the inside—with guanine always opposite cytosine and adenine always opposite thymine. In our staircase analogy, these base pairs are the stairsteps (**figure 25.6**). This structure can explain how cells are able to divide and go on functioning, how genetic data are passed on to new generations, and even how proteins are built to required specifications. It all depends on the base pairing.

Which brings up the still unanswered question "Why do the bases pair in that precise pattern, always A to T and T to A, always G to C and C to G?" The answer is hydrogen bonding and a truly elegant molecular design. **Figure 25.8** shows the two sets of base pairs. You should notice two things. First, a pyrimidine is paired with a purine in each case, and the long dimensions of both pairs are identical (1.085 nm). If two pyrimidines were paired or two purines were paired, the two pyrimidines would take up less space than a purine and a pyrimidine, and the two purines would take up more space, as is illustrated in **figure 25.9.** If this were the situation, the structure of DNA would be like a staircase made with stairs of different widths. In order for the two strands of the *double helix* to fit neatly, a pyrimidine must always be paired with a purine.

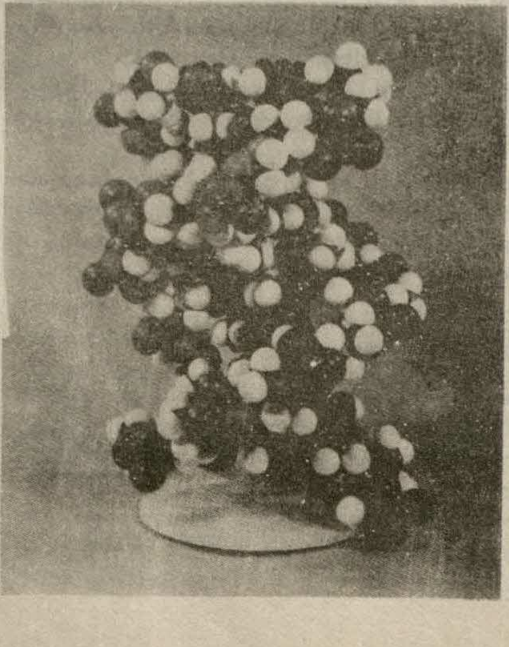


Figure 25.7 A model of the DNA molecule. (Courtesy of Science-Related Materials, Inc., Janesville, Wis.)

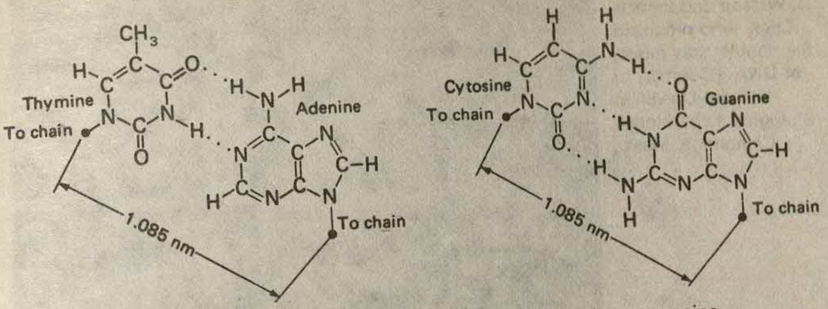
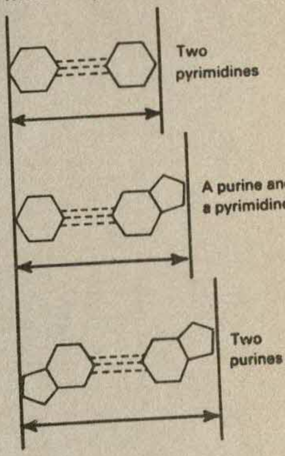


Figure 25.8 Base pairing of thymine to adenine and of cytosine to guanine.

Figure 25.9 Difference in widths of possible base pairs.



The other thing you should notice from **figure 25.8** is that when guanine is paired with cytosine, three hydrogen bonds can be drawn between the bases. No other pyrimidine-purine pairing will permit such extensive interaction. Indeed, in the pairing shown in the figure, both pairs of bases fit like lock and key.

There are about 10 base pairs per turn of the double helix. The acidic phosphate units are on the outside. In nucleoproteins, the highly basic proteins probably wrap around the double helix. Proton transfers from the phosphate units of DNA to the lysine and arginine side chains of the protein result in ionic charges. The protein is held to the nucleic acid, at least in part, by these salt bridges.

The molecules of RNA consist of single strands of the nucleic acid. Some internal (intramolecular) base pairing may occur in sections where the molecule folds back on itself. Because of this, portions of the molecule may exist in a double-helical form (**figure 25.10**). The importance of base pairing to the proper functioning of the various types of RNA will be shown in later sections.

Watson and Crick received the Nobel Prize in 1962 for discovering, as Crick put it, "the secret of life." It was not long after the development of the models that DNA was synthesized in the laboratory. In 1967, Arthur Kornberg, of Stanford University, carried out a test-tube synthesis of a single strand of DNA which was able to reproduce itself. Synthesis of life in a test tube? Almost, perhaps, but still a long way from a complete functioning cell.

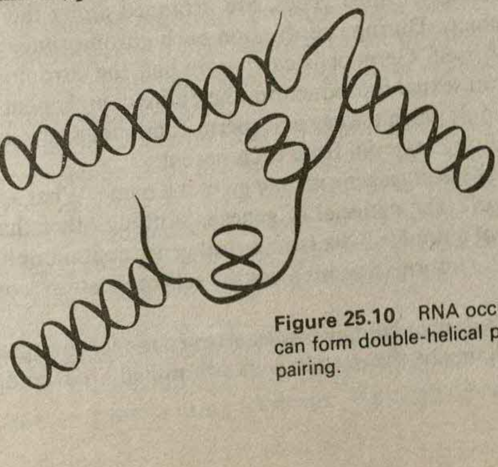


Figure 25.10 RNA occurs as single strands which can form double-helical portions by internal base pairing.

Figure 25.11 James D. Watson and Francis Crick, who proposed the double helix model of DNA. (Courtesy of Harvard University Biological Laboratories, Cambridge, Mass.)

25.6 DNA: Self-Replication of Cats and Cows and Kangaroos

Cats have kittens that grow up to be cats. Cows have calves that grow up to be cows. Why is it always so that each species reproduces after its own kind? How does a fertilized egg "know" that it should develop as a kangaroo and not as a koala bear?

The physical basis of heredity has been known for a long time. Most higher organisms reproduce sexually. A sperm cell from the male unites with an egg cell from the female. The fertilized egg so formed must carry all the information needed to make all the various cells, tissues, and organs necessary for the functioning of the new individual. For humans, that single cell must carry the information for the making of legs, livers, and lungs and heart, head, hair, and hands—in short, all the instructions ever needed for growth and maintenance of the individual. In addition, if the species is to survive, information must be set aside in germ cells—either sperm or eggs—for the production of new individuals.

The basic hereditary material is found in the nuclei of all cells, concentrated in elongated, threadlike bodies called chromosomes (**figure 25.12**). The number of chromosomes varies with the species. Human body cells have 46. The basic units of heredity, called genes, are arranged along the chromosomes in a linear fashion. During cell division each chromosome produces an exact duplicate of itself. Germ cells carry only half the chromosomes of the body cells. Thus, in sexual reproduction, the entire complement of chromosomes is achieved only when the egg and sperm combine; a new individual receives half its hereditary material from each parent.

Calling the unit of heredity a gene merely gives it a name. What are genes? What are they made of? The material of genes is nothing other than DNA arranged in the form of a double helix (some viral genes contain only RNA). Transmission of genetic information involves the self-replication (copying or duplication) of DNA.

The Watson-Crick double helix provides a ready model for genetic replication. If the two chains of the double helix are pulled apart and the hy-

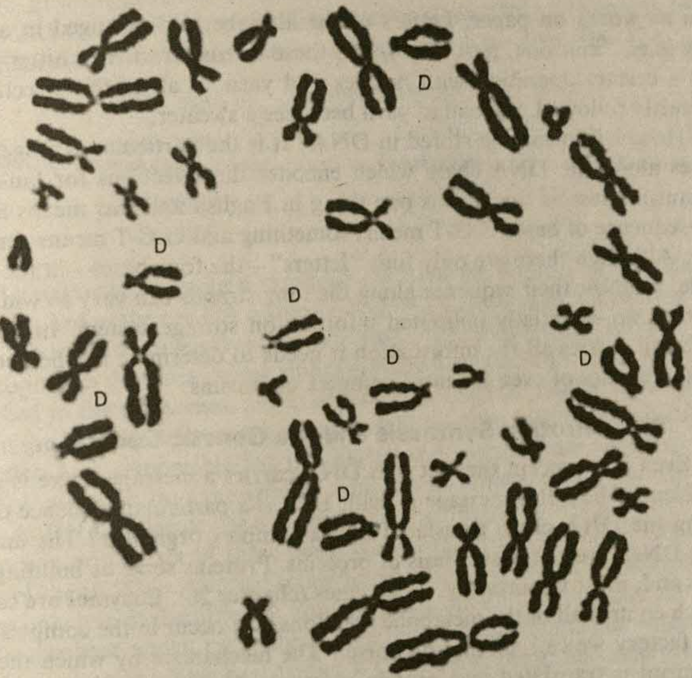


Figure 25.12 Human chromosomes in the metaphase stage, just before division. Note that there are 47 chromosomes instead of the normal 46. This cell came from a boy who had an extra chromosome number 13. Since numbers 13, 14, and 15 are indistinguishable in this photograph, they are all labeled D, and there are 7 D chromosomes instead of the expected 6. (Courtesy of Eeva Therman, University of Wisconsin, Madison.)

drogen bonds holding the base pairs together are broken, then each chain can direct the synthesis of a new DNA chain. In the cellular fluid surrounding the DNA are all the necessary nucleotides (monomers). It is simply a matter of a nucleotide with the proper base pairing with its complementary base on the DNA strand (**figure 25.13**). Keep in mind that adenine can pair only with thymine and guanine only with cytosine. Each base unit in the separated strand can pick up only a unit identical to the one that it had before. Each of the separating chains serves as a template, or pattern, for the formation of a new complementary chain.

As the nucleotides become aligned, they react with one another to form the polyester backbone of the new chain. In this way, each strand of the original DNA molecule forms a duplicate of its former partner. Whatever information was encoded in the original DNA double helix is now contained in each of the replicates. When the cell divides, each daughter cell gets one of the DNA molecules and all of the information which was available to the parent cell.

We keep saying that there is information encoded in the DNA molecule. DNA is often compared to a set of directions for putting together a model airplane or for knitting a sweater. Knitting directions store information as words on paper. Letters of the alphabet are arranged in a certain way (e.g., "knit one, purl two"), and these words direct the knitter to carry out a certain operation with needles and yarn. If all of the directions are correctly followed, the ball of yarn becomes a sweater.

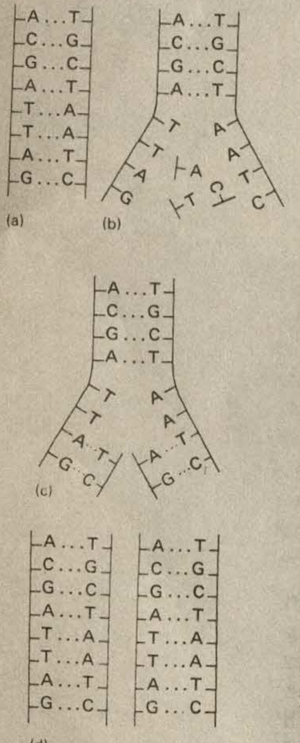
How is information stored in DNA? It is the particular arrangement of bases along the DNA chain which encodes the directions for building an organism. Just as *saw* means one thing in English and *was* means another, the sequence of bases C-G-T means something and G-C-T means something else. Although there are only four "letters"—the four bases—in the genetic code of DNA, their sequence along the long strands can vary so widely that there is an essentially unlimited information storage system. In its DNA, each cell carries all the information it needs to determine all the hereditary characteristics of even the most complex organisms.

25.7 RNA: Protein Synthesis and the Genetic Code

Even if we accept the fact that DNA carries a message, there is still the problem of how this message is read. How is a particular sequence of bases along the DNA chain translated into a complex organism? The answer is that DNA directs the synthesis of proteins. Proteins serve as building materials and, most importantly, as enzymes (chapter 26). Enzymes are catalysts which control all of the metabolic reactions that occur in the complex chemical factory we call a living organism. The mechanism by which the DNA blueprint is translated into protein molecules involves the intermediacy of RNA molecules.

In the first step, a portion of the DNA message is transcribed to a special kind of RNA, called messenger RNA (mRNA). (This is a little like xeroxing the directions for making a door from a library book which describes how to build an entire house.) One can envision a DNA double helix partially unzipping and then a limited portion of one DNA strand directing the synthesis of the single-stranded mRNA molecule (**figure 25.14**). Once again, the process involves a buildup of complementary nucleotides along the single DNA strand. The base sequence of DNA specifies the base sequence of mRNA. Thymine in DNA calls for adenine in mRNA, cytosine specifies

Figure 25.13 DNA replication. (a) The original double helix, flattened out here for clarity. (b) The helix beginning to split. Some free nucleotides from the cell are shown. (c) Nucleotides from the cell beginning to pair with bases on each original strand. (d) The two new double helices, each identical to the original.



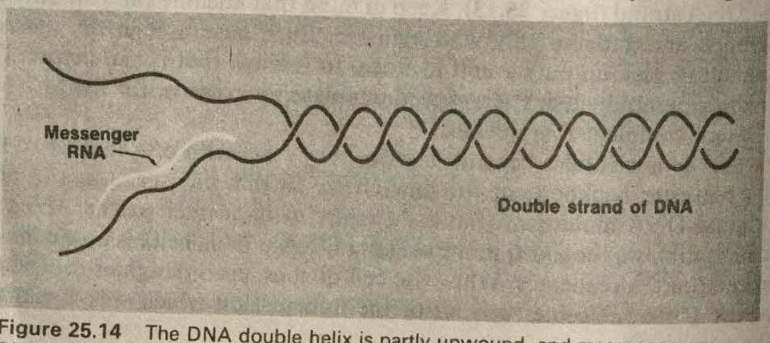
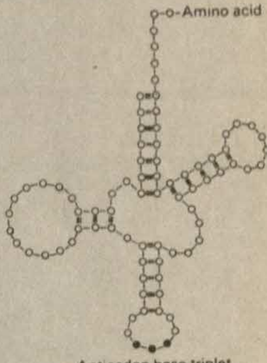


Figure 25.14 The DNA double helix is partly unwound, and messenger RNA is formed on the separate portion. (Reprinted with permission from Jones, Mark M., Netterville, John T., Johnston, David O., and Wood, James L., *Chemistry, Man, and Society*, Philadelphia: W. B. Saunders, 1972. Copyright © 1972 by W. B. Saunders.)

guanine, guanine calls for cytosine, and adenine requires uracil. Recall from section 25.1 that, in RNA molecules, uracil replaces DNA's thymine. Notice the similarity between the structures of these two bases (pp. 516–17).

DNA Base	*Complementary RNA Base*
Adenine	Uracil
Thymine	Adenine
Cytosine	Guanine
Guanine	Cytosine

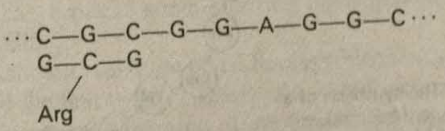
Figure 25.15 A given transfer RNA can carry only one kind of amino acid, which is specified by the base triplet in the anticodon.



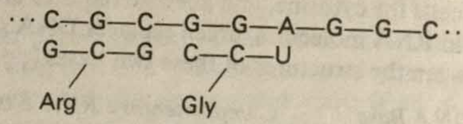
The next step in protein synthesis involves the reading of the blueprint now encoded in the mRNA molecule and its translation into a protein structure. The mRNA travels from the nucleus to the cytoplasm of the cell, where nucleoprotein granules called ribosomes are located. The mRNA becomes attached to the ribosomes, and it is here that the genetic code is deciphered.

In the cytoplasm is another kind of RNA, called transfer RNA (tRNA). The tRNA is responsible for translating the specific base sequence of an mRNA molecule into the specific amino acid sequence of a protein molecule. A tRNA molecule has a looped structure (**figure 25.15**). On one of these loops is a critical set of three bases (called the triplet). One of the trailing ends of the tRNA is attached to an amino acid. A given tRNA molecule can carry only one of the different amino acids. And all tRNA molecules with a particular base triplet carry the same kind of amino acid. For example, all tRNA molecules whose base triplet is CCU carry the amino acid glycine. A tRNA molecule with the base triplet GCG always has an arginine molecule attached. There are many more ways of sequencing three bases than there are kinds of amino acids. Thus, one kind of amino acid is usually associated with more than one triplet sequence, so that a tRNA molecule with a CCG triplet, as well as one with a CCU triplet, may carry glycine. What is important is that a specific pattern of bases is associated with a specific pattern of amino acids.

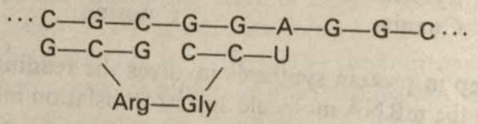
We are now ready to build proteins. Strung out along some ribosomes in the cytoplasm of a cell is an mRNA molecule. The sequence of bases along this molecule was determined by the DNA of a gene in the cell nucleus. Floating around in the cytoplasm surrounding the mRNA are tRNA molecules, each carrying its own amino acid. Let us suppose that a portion of the mRNA base sequence reads ···C-G-C-G-G-A-G-G-C···. The first three bases (C-G-C) could pair, through hydrogen bonding, with a nucleic acid that had a G-C-G sequence. There, floating around in the cytoplasm, is just such a nucleic acid, a tRNA molecule with the amino acid arginine attached. This tRNA pairs up with the first three bases of the mRNA.



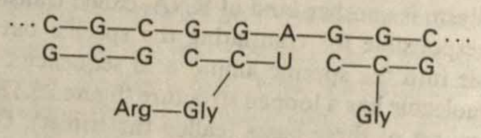
The next three bases of the mRNA, G-G-A, will pair up with a C-C-U tRNA molecule, which carries the amino acid glycine.



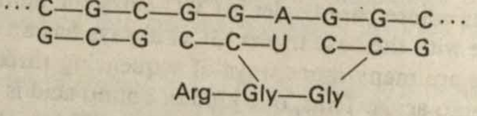
When the two tRNA molecules are appropriately lined up along the mRNA, a peptide bond forms between the two amino acids.



The next three bases on the mRNA (G-G-C) pair with a C-C-G tRNA molecule.



The amino acid carried by the tRNA is then joined by a peptide bond to the previously linked amino acids.



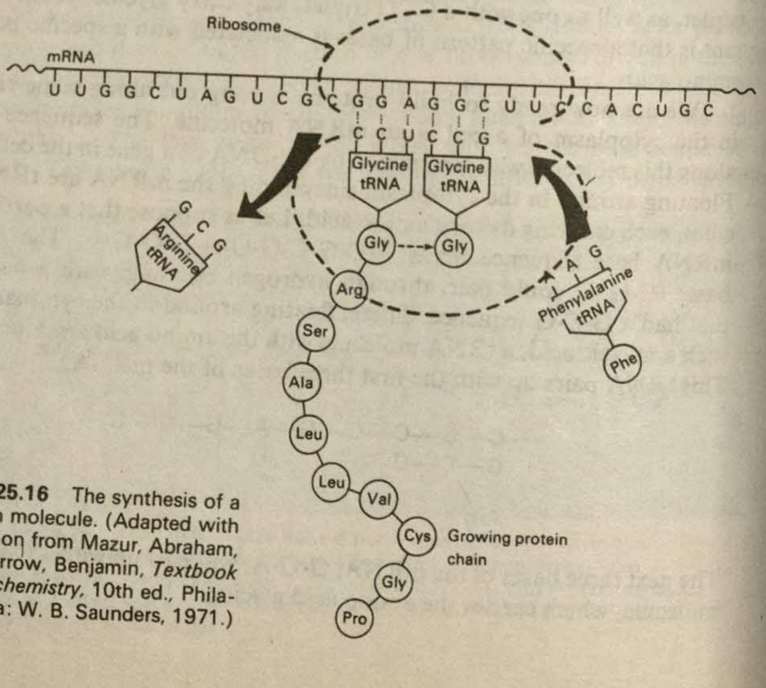


Figure 25.16 The synthesis of a protein molecule. (Adapted with permission from Mazur, Abraham, and Harrow, Benjamin, *Textbook of Biochemistry*, 10th ed., Philadelphia: W. B. Saunders, 1971.)

	Second base								
First base	U		C		A		G		Third base
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Cys	C
	UUA	Leu	UCA	Ser	UAA	Stop	UGA	Stop	A
	UUG	Leu	UCG	Ser	UAG	Stop	UGG	Try	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC	Leu	CCC	Pro	CAC	His	CGC	Arg	C
	CUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg	A
	CUG	Leu	CCG	Pro	CAG	Gln	CGG	Arg	G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC	Ile	ACC	Thr	AAC	Asn	AGC	Ser	C
	AUA	Ile	ACA	Thr	AAA	Lys	AGA	Arg	A
	AUG	Met	ACG	Thr	AAG	Lys	AGG	Arg	G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC	Val	GCC	Ala	GAC	Asp	GGC	Gly	C
	GUA	Val	GCA	Ala	GAA	Glu	GGA	Gly	A
	GUG	Val	GCG	Ala	GAG	Glu	GGG	Gly	G

Figure 25.17 The genetic code for protein synthesis.

In this way the protein chain is gradually built up. The chain is released from the tRNA and mRNA as it is formed (**figure 25.16**).

Each base triplet strung consecutively along the *mRNA* molecule is called a *codon*. The base triplets of the *tRNA* molecules are called *anticodons*. A codon on mRNA always pairs with its complementary tRNA anticodon. A complete dictionary of the genetic code has been compiled. **Figure 25.17** shows which amino acids are called for by all the possible mRNA codons. The amino acids serine and leucine are each specified by six different codons. Two amino acids, tryptophan and methionine, have only one codon each. Note that three codons, UAA, UAG, and UGA are stop signals, calling for termination of the protein chain.

All proteins for muscle, hair, skin, and the all-important enzymes are formed by the mechanism just outlined. Next time you look in a mirror, remember that what you see depends ultimately on something as fragile as a hydrogen bond.

25.8 Bioethics

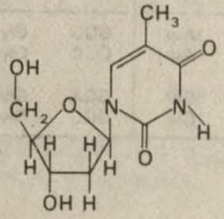
Knowledge gives power. It does not necessarily give wisdom. The new molecular genetics has brought some startling developments—and some mindboggling possibilities.

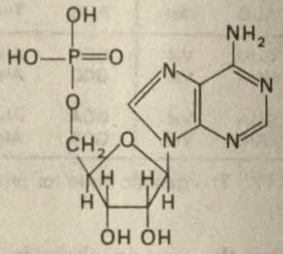
In 1976, a Massachusetts Institute of Technology biochemist, H. Gobind Khorana, announced the first total synthesis of a fully functional gene. The door to the manipulation and alteration of our genetic heritage was opened a little wider. The door will open to a new world of promise—elimination of genetic defects, a cure for cancer, a race of geniuses, and who knows what? But the door will also open to new problems—a lower death rate in an already crowded world, differing opinions on what sort of creatures the human species should be, perhaps even perils as yet unimagined. The greatest of all problems will most likely be that of choosing who is to play "God" with the new "secret of life."

Figure 25.18 H. Gobind Khorana. (Courtesy of the Massachusetts Institute of Technology, Cambridge.)

Problems

1. What are the differences in RNA and DNA in terms of the following?
   a. bases present
   b. sugars present
   c. function
   d. secondary structure
2. What base and what sugar are present in each nucleoside?
   a. adenosine
   b. deoxyguanosine
   c. uridine
   d. cytidine
3. For each compound specify whether the molecule is a nucleic acid, a nucleotide, or a nucleoside, whether the base is a pyrimidine or a purine, and, on the basis of the sugar unit, whether the molecule would be incorporated ultimately into RNA or DNA.





4. What is the difference between AMP, ADP, ATP, and cyclic AMP?
5. Using **figure 25.8** as a guide, show the hydrogen bonding between uracil and adenine.
6. Using **figure 25.8** as a guide, pair cytosine with adenine and thymine with guanine and evaluate the possibility for hydrogen bonding. Are the interactions greater or less than for the correct C-G and A-T pairings?
7. Using a schematic representation, show the design of the double helix. Indicate the positions of the sugar, phosphoric acid, and base units.
8. How does DNA replicate itself?
9. How does DNA control protein synthesis? What are the roles of messenger RNA and transfer RNA?
10. Chemical bonds can be broken by ultraviolet radiation, gamma rays, cosmic rays, and certain chemical substances. What are the biological implications of these facts? (Hint: What effect might the breaking of chemical bonds have on DNA?)

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chapter 26

Enzymes and Coenzymes

Enzymes are a highly specialized class of proteins. They control and direct the myriad of chemical reactions that occur in living cells. Enzymes are biological catalysts produced by cells but able to act independently of the cells. For example, an enzyme isolated from the cell that made it will still catalyze reactions, even in a test tube or a laundry tub.

Enzymes have enormous catalytic power. They speed up reactions by factors of a 1 000 000 or more. Most reactions in living cells would be imperceptibly slow without enzymes. Even a simple reaction like the conversion of carbon dioxide to carbonic acid is catalyzed by an enzyme.

$$CO_2 + H_2O \xrightleftharpoons{\text{enzyme}} H_2CO_3$$

Without the enzyme, the body tissues couldn't dump carbon dioxide into the blood fast enough. The enzyme, called carbonic anhydrase, speeds up the reaction by a factor of 10 000 000! Each enzyme molecule can convert 100 000 molecules of carbon dioxide per second.

About two thousand enzymes are known. Many are available commercially in varying grades of purity. Some have even been isolated as highly purified crystals.

26.1 The Anatomy of Enzymes

All known enzymes are proteins. As such, they can be considered according to their primary structure (their amino acid sequence) and their secondary, tertiary, and quaternary features. The primary structure of the protein hormone insulin (chapter 27) was determined by Frederick Sanger in 1953. Shortly thereafter many researchers began to determine the amino acid sequences of proteins, including some enzymes.

The first enzyme to have its three-dimensional structure determined was lysozyme. The amino acid sequence of this protein was determined inde-

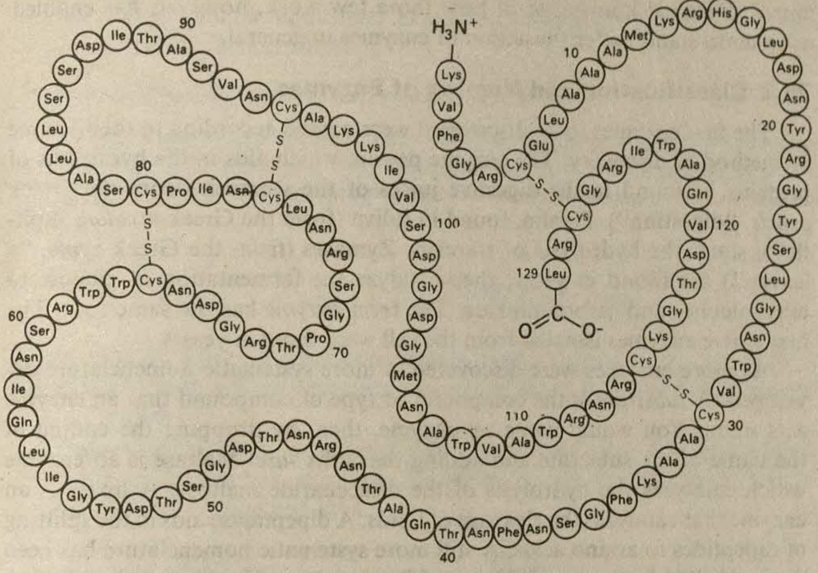


Figure 26.1 The primary structure of egg white lysozyme. (Reprinted with permission from Stryer, Lubert, *Biochemistry*, San Francisco: W. H. Freeman and Company, 1975. Copyright © 1975 by Lubert Stryer. Adapted with permission from Canfield, R. E., and Liu, A. K., "The Disulfide Bonds of the Egg White Lysozyme (Muramidase)," *Journal of Biological Chemistry*, May 1965, and Phillips, David C., "The Three-dimensional Structure of an Enzyme Molecule," *Scientific American*, November 1966.)

pendently by Pierre Jolles and coworkers at the University of Paris and by Robert Canfield, of Columbia University, in 1963. Lysozyme, obtained from egg white, is composed of a single polypeptide chain of 129 amino acid units. The chain is cross-linked at four locations by disulfide bonds (**figure 26.1**).

Lysozyme breaks down the cell walls of bacteria. Its mode of action, however, cannot be understood from its primary structure alone. The three-dimensional structure, determined by the folds in the molecule, must be known in order for the properties of the molecule to be understood. This three-dimensional structure was worked out by David C. Phillips and coworkers at the Royal Institution in London in 1965. The skeleton of this structure is shown in **figure 26.2**. What looks like an apparently random orientation of the chain is actually a precise folding which is exactly repeated in every molecule of the active enzyme.

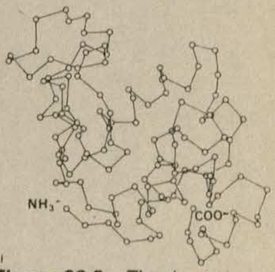


Figure 26.2 The three-dimensional structure of lysozyme, showing only the C—C—N skelton. (Courtesy of David C. Phillips, Oxford University, Oxford.)

With the structure of lysozyme known, it was possible to determine how it functions. The bacterial cell wall is composed of a polysaccharide. A portion of the polysaccharide attaches itself to a specific portion of the lysosyme molecule. That portion of the enzyme has glutamic acid and aspartic acid residues. These interact with the acetal linkage of the polysaccharide, breaking the bond. When enough of these acetal linkages cleave, the bacterial cell wall ruptures.

Three-dimensional structures of only a few enzymes have been determined. Detailed knowledge of how those few work, however, has enabled us to understand better the action of enzymes in general.

26.2 Classification and Naming of Enzymes

The first enzymes to be discovered were named according to their source or method of discovery. The enzyme pepsin, which aids in the hydrolysis of proteins, is found in the digestive juices of the stomach (from the Greek *pepsis,* "digestion"). Ptyalin, found in saliva (from the Greek *ptyalon,* "spittle"), starts the hydrolysis of starches. Zymases (from the Greek *zyme,* "a leaven") are found in yeast; they catalyze the fermentation of glucose to ethyl alcohol and carbon dioxide. The term *enzyme* has the same root. The first active enzymes isolated from the cell were those in yeasts.

As more enzymes were discovered, a more systematic nomenclature developed. A *substrate* is the compound or type of compound that an enzyme acts upon. You would name an enzyme, then, by dropping the ending of the name of the substrate and adding the suffix *-ase*. Maltase is an enzyme which catalyzes the hydrolysis of the disaccharide maltose. A lipase is an enzyme that catalyzes the cleavage of lipids. A dipeptidase aids in the splitting of dipeptides to amino acids. A still more systematic nomenclature has been devised by the International Union of Biochemistry. Used mainly by research workers, that system will not be discussed further here. Those interested can consult reference 8 (pp. 303–8).

Enzymes are generally classified according to the *type* of chemical reaction that they catalyze. There are six major types.

1. *Hydrolases* are enzymes that catalyze hydrolysis reactions. These include *lipases,* which act on fat and other lipids, *carbohydrases,* which speed up the hydrolysis of carbohydrates to monosaccharides, and *proteases* and *peptidases,* which catalyze the hydrolysis of proteins and peptides.
2. *Oxidases* operate in physiological oxidation reactions. They are essential in cells which use oxygen to produce energy. This group includes the *dehydrogenases,* enzymes which oxidize by the removal of hydrogen. For example, alcohol dehydrogenase speeds the oxidation of ethanol to acetaldehyde.

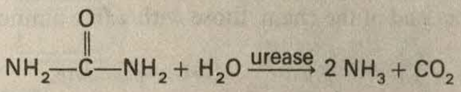
$$CH_3CH_2OH \longrightarrow CH_3CHO + \text{"2 H"}$$

3. *Transferases* facilitate the transfer of groups such as methyl, amino, and acetyl from one molecule to another. *Transaminase* catalyzes the transfer of an amino group from one molecule to another. This reaction is involved in the removal of the amino group during the metabolism of amino acids (chapter 32). *Kinases* are involved in the transfer of phosphate groups.
4. *Lyases* aid in the removal of certain groups without hydrolysis. Examples are the *decarboxylases,* which catalyze the removal of carboxyl groups.
5. *Isomerases,* as their name implies, catalyze the conversion of a compound into another which is isomeric with it.
6. *Ligases* or *synthetases* are involved in the formation of new bonds from carbon to a nitrogen, an oxygen, a sulfur, or another carbon atom.

We will encounter additional examples, particularly of the first four classes, in subsequent chapters.

26.3 Precision Proteins: Enzyme Specificity

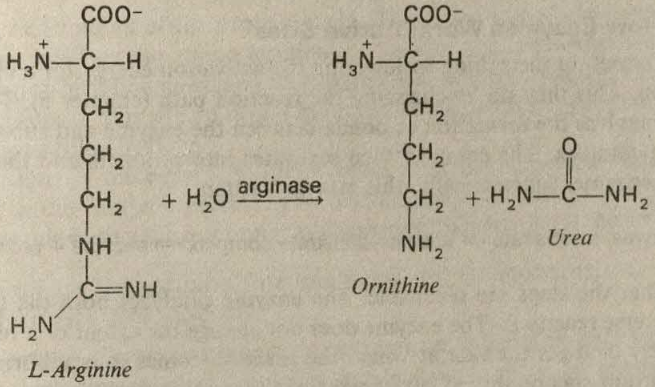
Enzymes are highly specific. They catalyze only one reaction or a group of closely related reactions. For example, the enzyme *urease* catalyzes a single reaction, the hydrolysis of urea.



$$NH_2-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2 + H_2O \xrightarrow{\text{urease}} 2\,NH_3 + CO_2$$

Urease has no effect on other compounds, even closely related ones such as the amides. Such *absolute specificity* is rather rare among enzymes characterized to date.

Many enzymes show *stereospecificity*. These react with only one of a pair of mirror image isomers. *Arginase*, for example, catalyzes the hydrolysis of L-arginine to ornithine and urea.



On the other hand, arginase has no effect on the rate of hydrolysis of D-arginine.

Other enzymes are *reaction specific*. Those that catalyze the hydrolysis of peptide linkages might also catalyze the hydrolysis of closely related ester linkages but would do so with less efficiency. Some enzymes are highly *linkage* specific. *Trypsin*, for example, splits only those peptide bonds on the carboxyl side of lysine and arginine units in proteins.

$$\cdots \text{Arg}-\text{xxx}\cdots + H_2O \xrightarrow{\text{trypsin}} \cdots \text{Arg}-COO^- + H_3\overset{+}{N}-\text{xxx}\cdots$$

$$\cdots \text{Lys}-\text{xxx}\cdots + H_2O \xrightarrow{\text{trypsin}} \cdots \text{Lys}-COO^- + H_3\overset{+}{N}-\text{xxx}\cdots$$

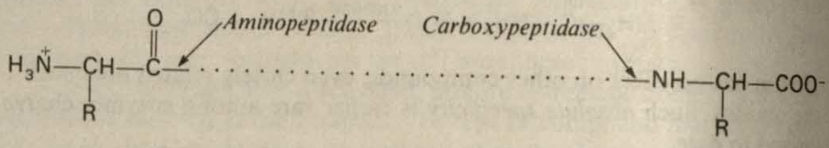
Thrombin is even more specific. It cleaves only those bonds between arginine and glycine.

$$\cdots \text{Arg}-\text{Gly}\cdots + H_2O \xrightarrow{\text{thrombin}} \cdots \text{Arg}-COO^- + H_3\overset{+}{N}-\text{Gly}\cdots$$

Thrombin has no effect on the hydrolysis of other peptide linkages. It won't even attack the bonds between glycine and arginine if the order is reversed.

$$\cdots \text{Gly—Arg} \cdots + H_2O \overset{\text{thrombin}}{\not\longrightarrow} \text{no reaction}$$

Another kind of specificity is *group specificity*. *Carboxypeptidase*, for example, cleaves only those terminal amino acids at the end of a protein chain which has a free carboxyl group. *Aminopeptidase*, on the other hand, cleaves those at the other end of the chain, those with a free amino group.



Enzyme specificity is crucial in chemical reactions in the cell. It ensures, for the most part, that the proper reactions occur in the proper place at the proper time.

26.4 How Enzymes Work: Active Sites

Enzymes do their thing by lowering the activation energy for a chemical reaction. This they do by changing the reaction path (chapter 5). The new route involves the formation of bonds between the enzyme and substrate to form a complex. The complex then separates into products and the regenerated enzyme. Schematically, this may be written

$$\text{Enzyme} + \text{substrate} \rightleftarrows \text{enzyme-substrate complex} \rightleftarrows \text{enzyme} + \text{product}$$

Note that the steps are reversible. The enzyme catalyzes both the forward and reverse reactions. The enzyme does not change the extent of a reaction; it merely changes the rate at which the reaction comes to equilibrium. An equilibrium may be shifted left or right by the usual factors (chapter 5), such as temperature, concentration of reactant and product, or removal of a reactant or product.

Enzyme action is often explained by a lock-and-key analogy. The substrate must fit a portion of the enzyme, called the *active site*, quite precisely (**figure 26.3**), just as a key must fit a tumbler lock in order to open it.

Not only must the enzyme and substrate fit precisely, but they are probably held together by electrical attraction. That requires that certain charged groups on the enzyme complement certain charged or partially charged groups on the substrate. Formation of new bonds to the enzyme by the substrate probably weakens bonds within the substrate. The bonds in the substrate can then be easily broken.

The active site on an enzyme is usually rather small, and only that small part comes into direct contact with the substrate. Side chains of amino acid units, usually those containing amino, carboxyl, or sulfhydryl groups, are often involved. The amino acid units involved need not be next to one another in the primary sequence. They must, however, be brought close by the cross-

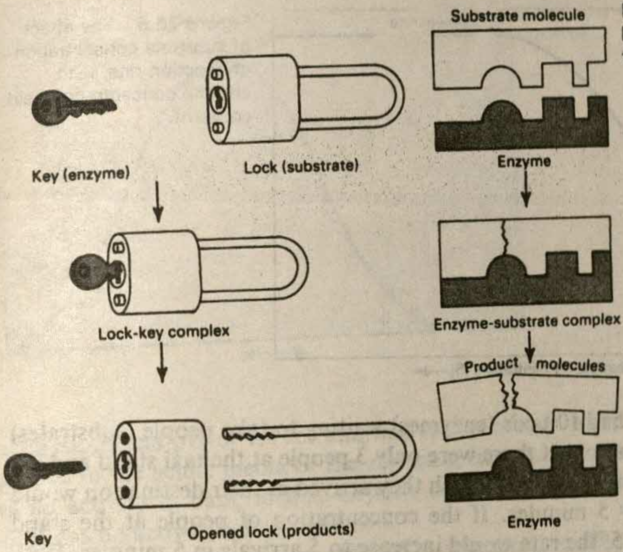


Figure 26.3 The lock-and-key model for enzyme action.

linking and folding of the protein chain. The active site of *chymotrypsin*, a protease, involves the amino terminal of the chain, a cross-linked loop incorporating histidine units, and an aspartic acid side chain (**figure 26.4**). The polar groups at this site no doubt interact strongly with the peptide linkage which is to be hydrolyzed.

Portions of the enzyme molecule other than the active site may be involved in the catalytic process. The rearrangement of these other parts of the molecule during the reaction may cause essential changes at the active site.

26.5 Factors Influencing Enzyme Activity: Concentration, Temperature, and pH

The rates of reactions involving enzymes are influenced by a variety of factors, including concentration of substrate, concentration of enzyme, temperature, and the pH of the medium. The enzyme and substrate must come together for the reaction to take place. The chance of this meeting depends on the concentration of each substance. If the concentration of substrate, [S], is varied, the reaction rate will increase as [S] increases (**figure 26.5**). Eventually, a concentration is reached which saturates all the active sites on the enzymes. The rate levels off; further increase in concentration of substrate leaves the rate unchanged.

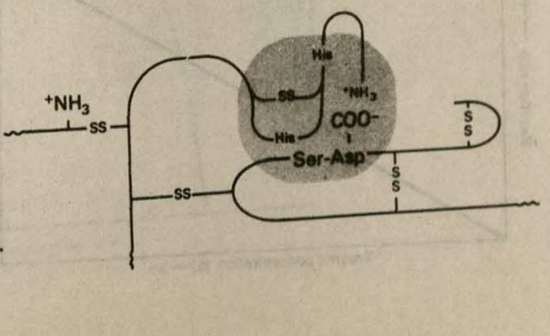


Figure 26.4 A diagram of a portion of a chymotrypsin molecule, showing the active site.

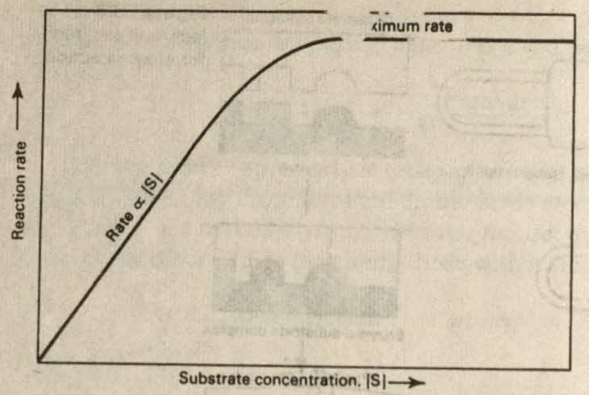


Figure 26.5 The effect of substrate concentration on reaction rate, with enzyme concentration held constant.

It is as if you had 10 taxis (enzymes) waiting to take people (substrates) to a certain destination. If there were only 3 people at the taxi stand and the trip took 5 minutes, the rate at which they arrived at their destination would be 3 people every 5 minutes. If the concentration of people at the stand were increased to 5, the rate would increase to 5 arrivals in 5 minutes. With 10 people, you would have 10 arrivals every 5 minutes. With 20 people at the stand, the rate would still be 10 arrivals in 5 minutes. The taxis have been saturated (in our analogy, each taxi can carry only one passenger). If the taxis could carry 2 or 3 passengers each, the same principle would apply. The rate would simply be higher (20 or 30 people in 5 minutes) before it leveled off.

If the concentration of substrate is held constant and remains in excess (if we always have more people than taxis), the rate of a reaction is proportional to the concentration of enzyme. The more enzyme, the faster the reaction (the more taxis, the more people can be transferred). This relationship holds over a wide range of enzyme concentrations (**figure 26.6**).

Enzymes are proteins with acidic and basic groups. It is not surprising, therefore, that enzyme activity is influenced by the concentration of hydrogen ions. Each enzyme has its own *optimum pH*. If a graph is plotted of reaction rate versus pH, the curve will show a sharp decline on both sides of some optimum value (**figure 26.7**). The optimum pH is generally close to

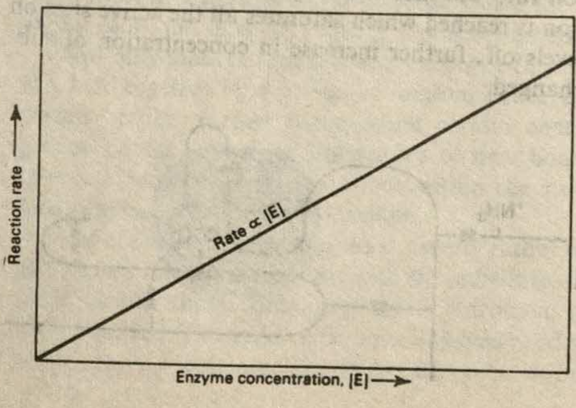


Figure 26.6 The effect of enzyme concentration on reaction rate, with the concentration of substrate constant and in excess.

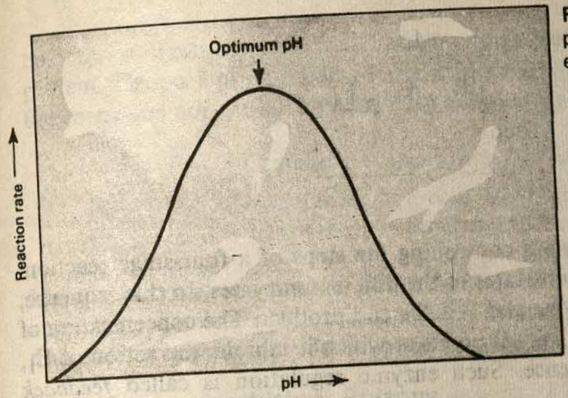


Figure 26.7 The effect of pH on the activity of an enzyme.

the physiological pH of 7.4 for enzymes in the human body. Pepsin, which operates in the acidic media of the stomach, has an optimum pH of 1.6. It has no activity in basic media. Glycine oxidase operates best at a pH of 8.8. It has no activity below a pH of 5.

Reaction rates generally are affected by temperature. The higher the temperature, the faster the reaction. This is also true for reactions catalyzed by enzymes—up to a point. Enzymes are proteins. Proteins are denatured by higher temperatures, and their enzymatic activity is destroyed. The temperature range for activity of enzymes generally is 10 to 50 °C. The *optimum temperature* for many enzymes in the human body is 37 °C—body temperature (**figure 26.8**).

26.6 Negative Feedback: Nature's Stop Sign

Most biochemical processes involve several steps, each catalyzed by an enzyme, in which the product of one step becomes the substrate for the next enzyme. Generally, the first enzyme of the sequence regulates the rate of the entire set. It is called the *allosteric* or *regulatory* enzyme. How does this enzyme know when to shut off? Generally it is inhibited by the end product.

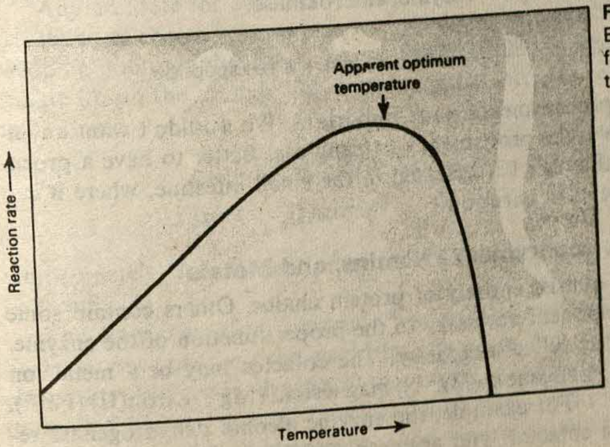
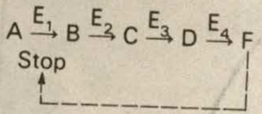


Figure 26.8 Enzyme activity as a function of temperature.

Schematically, this can be diagrammed as



The *E*s are various enzymes controlling the steps of a four-stage reaction. *A* through *D* represent substrates of the different enzymes. In this sequence, E_1 is the regulatory enzyme and F is the end product. The concentration of F builds up to a certain critical point. at which it inhibits the action of E_1, thus stopping the sequence. Such enzyme regulation is called *feedback inhibition.*

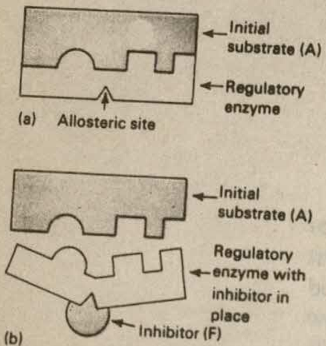


Figure 26.9 A model for the action of a regulatory enzyme. (a). The regulatory enzyme and its substrate fit like lock and key. (b) With the inhibitor bound at the allosteric site, the active site of the regulatory enzyme is distorted, and the regulatory enzyme will not bind its substrate.

Regulatory enzymes are generally larger molecules than the other enzymes in the set. In addition to having active sites for the regular substrate, they also have *allosteric sites* which bind the inhibitor. This changes the conformation, and hence the activity, of the enzyme.

26.7 Proenzymes: Activation of Enzyme Precursors

A protein called *pepsinogen* is secreted from the cells of the stomach. The acid in the stomach converts pepsinogen into pepsin, an active proteinase. The reaction is also *autocatalytic*: it is catalyzed by the product pepsin. That is, once some pepsin is formed, it speeds the reaction, which produces more pepsin. Activation involves removal of 42 amino acid residues, as small peptides, from the pepsinogen molecule.

$$\text{Pepsinogen} + H_3O^+ \xrightarrow{\text{pepsin}} \text{pepsin} + \text{small peptides}$$

Substances such as pepsinogen, which are not enzymes but which are converted into enzymes by other substances, are called *proenzymes.*

Another proenzyme is *trypsinogen,* formed in the pancreas. It is converted into *trypsin* by the removal of a hexapeptide from the amino end. This activation is itself catalyzed by an enzyme, enterokinase.

$$\text{Trypsinogen} \xrightarrow{\text{enterokinase}} \text{trypsin} + \text{a hexapeptide}$$

Activation of proenzymes is quite important. We wouldn't want an enzyme breaking down the proteins of our pancreas. Better to have a proenzyme made there that can be activated in the small intestine, where it can hydrolyze the proteins in our food.

26.8 Cofactors: Coenzymes, Vitamins, and Metals

Some enzymes consist entirely of protein chains. Others contain some other chemical component necessary to the proper function of the enzyme. Such a component is called a *cofactor*. The cofactor may be a metal ion such as zinc (Zn^{2+}), manganese (Mn^{2+}), magnesium (Mg^{2+}), iron(II) (Fe^{2+}), or copper(II) (Cu^{2+}). For example, the enzyme alcohol dehydrogenase requires zinc ion as a cofactor, and arginase requires manganese ion. If the cofactor is organic in nature, it is called a *coenzyme*. Coenzymes are nonprotein. The pure protein part of an enzyme is called an *apoenzyme*. Neither the coenzyme nor the apoenzyme have enzymatic activity alone.

$$\underset{\substack{\textit{Nonprotein}\\ \textit{(inactive)}}}{\text{Coenzyme}} + \underset{\substack{\textit{Protein}\\ \textit{(inactive)}}}{\text{apoenzyme}} \longrightarrow \underset{\textit{(Active)}}{\text{enzyme}}$$

Many coenzymes are vitamins or are derived from vitamin molecules. These important chemical substances and their relationships to vitamins will be discussed in considerable detail in the next chapter.

26.9 Enzyme Inhibition: Poisons

Poisons act in a variety of ways, but the most deadly of them act by inhibiting enzymes. This they may do by tying up an enzyme in the form of a stable complex, by denaturing it, or by blocking its formation from its apoenzyme and cofactor. Let's look at a few examples.

Cyanide is one of the most notorious poisons in both fact and fiction. It acts almost instantly, and only a minute amount is needed for a lethal dose. The average fatal dose is only 50 or 60 mg. Cyanide is used as gaseous hydrogen cyanide ($H—C\equiv N$) and as solid salts which contain the cyanide ion ($C\equiv N^-$). The gas is used (with great care by specially trained experts) for extermination of insects and rodents in ships, warehouses, and railway cars and on citrus and other fruit trees. Sodium cyanide ($NaCN$) is used in the extraction of gold and silver from their ores and in electroplating baths.

Cyanide blocks the oxidation of glucose inside a cell by forming a stable complex with the oxidation enzymes. The enzymes, called cytochrome oxidases, contain iron and copper atoms. They normally act by providing electrons for the reduction of oxygen in the cell. Cyanide ties up those mobile electrons, rendering them unavailable for the reduction process. Thus, cyanide brings an abrupt end to cellular respiration, causing death in a matter of minutes.

Any antidote for cyanide poisoning must be administered quickly. The treatment of choice nowadays is sodium thiosulfate (the "hypo" used in developing photographic film). The sulfur atom is transferred from the thiosulfate ion to the cyanide ion, converting the latter to relatively innocuous thiocyanate.

$$\underset{\textit{Cyanide}}{CN^-} + \underset{\textit{Thiosulfate}}{S_2O_3^{2-}} \longrightarrow \underset{\textit{Thiocyanate}}{SCN^-} + \underset{\textit{Sulfite}}{SO_3^{2-}}$$

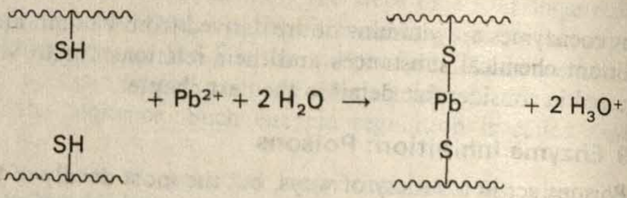
Unfortunately, few victims of cyanide poisoning survive long enough to be treated.

The active site of an enzyme often contains sulfhydryl groups (—SH). Such enzymes can be deactivated by any agent that changes these groups chemically. We saw in chapter 20 that mercury could deactivate enzymes by tying up sulfhydryl groups. Lead is another heavy metal poison. Recall that lead(II) ions react with hydrogen sulfide to form insoluble lead sulfide.

$$Pb^{2+} + H_2S + 2\,H_2O \longrightarrow PbS + 2\,H_3O^+$$

Lead(II) ion *Lead sulfide (insoluble)*

Similarly, lead ions react with the sulfhydryl groups of enzymes, rendering them inactive.



Enzymes with sulfhydryl groups *Enzyme (inactive)*

Compounds of the element lead are widespread in the environment, reflecting the many uses that we have for this soft, dense, corrosion-resistant metal and its compounds. Lead (as Pb^{2+}) is present in many foods, generally not exceeding 0.3 ppm. However, condensed milk, sold in cans sealed with lead solder, may contain as much as 0.5 ppm. Lead (again as Pb^{2+}) also gets into our water (in amounts of up to 0.1 ppm) from lead-sealed pipes. Lead compounds enter the air from the exhausts of cars using "leaded" gasoline.

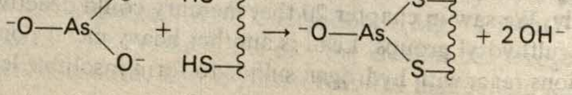
Lead compounds are quite toxic. Metallic lead is generally converted to lead(II) ions in the body. So, with all that lead, why aren't we dead? The answer lies in the fact that we can excrete about 2 mg per day. Our intake from air, food, and water is generally less than that. If intake exceeds excretion, lead builds up in the body, and chronic lead poisoning results.

Like mercury poisoning (chapter 20), lead poisoning can be treated with British Anti-Lewisite (BAL). The antidote of choice nowadays, however, is another chelating agent, ethylenediaminetetraacetic acid or EDTA (**figure 26.10**). The calcium salt of EDTA is administered intravenously. In the body, calcium ions are displaced by lead ions, which the chelate bonds more tightly.

$$CaEDTA^{2-} + Pb^{2+} \longrightarrow PbEDTA^{2-} + Ca^{2+}$$

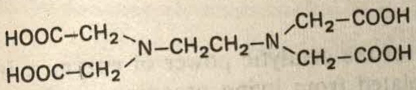
The lead-EDTA complex is excreted. As with mercury poisoning, the neurological damage done by lead poisoning is essentially irreversible. Treatment must be begun early to be effective.

The infamous poison arsenic is not a metal but has some metallic properties. In commercial poisons, arsenic is usually found as arsenate (AsO_4^{3-}) or arsenite (AsO_3^{3-}) ions. These ions also render enzymes inactive by tying up sulfhydryl groups.

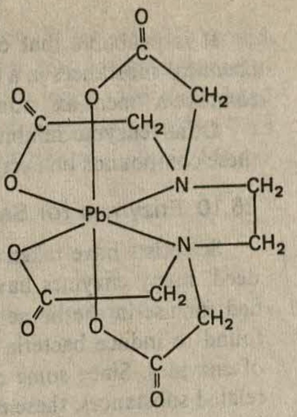


Arsenite ion *Enzyme* *Enzyme (inactive)*

Figure 26.10 EDTA and the complex that it forms with lead.

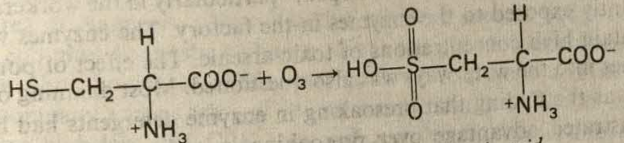


EDTA



Lead-EDTA complex

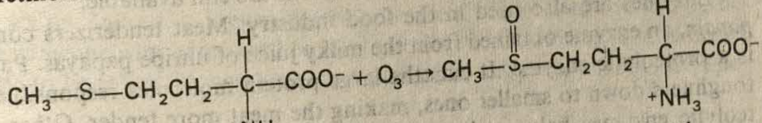
Enzymes can also be deactivated by oxidation. Ozone, peroxyacetyl nitrate (PAN), and other oxidizing components of photochemical smog probably do their main damage through the deactivation of enzymes. The active sites of enzymes often incorporate the sulfur-containing amino acids cysteine and methionine. Cysteine is readily oxidized by ozone to cysteic acid.



$$\mathrm{HS{-}CH_2{-}\overset{H}{\underset{{}^{+}NH_3}{C}}{-}COO^- + O_3 \rightarrow HO{-}\overset{O}{\underset{O}{S}}{-}CH_2{-}\overset{H}{\underset{{}^{+}NH_3}{C}}{-}COO^-}$$

Cysteine *Cysteic acid*

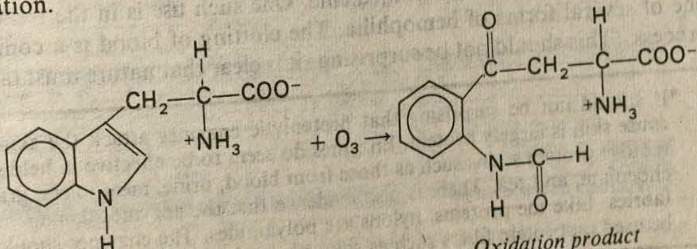
Methionine is oxidized to methionine sulfoxide.



$$\mathrm{CH_3{-}S{-}CH_2CH_2{-}\overset{H}{\underset{{}^{+}NH_3}{C}}{-}COO^- + O_3 \rightarrow CH_3{-}\overset{O}{S}{-}CH_2CH_2{-}\overset{H}{\underset{{}^{+}NH_3}{C}}{-}COO^-}$$

Methionine *Methionine sulfoxide*

Still another amino acid, tryptophan, is known to react with ozone. Tryptophan, which does not contain sulfur, undergoes a ring-opening oxidation.



Tryptophan *Oxidation product*

It is probable that oxidizing agents can break bonds in many of the chemical substances in a cell. Such powerful agents as ozone are more likely to make a "meat-ax" attack than to react in a highly specific way.

Other enzyme inhibitors include the organophosphates. The action of these compounds on acetylcholinesterase was discussed in chapter 20.

26.10 Enzymes for Sale

Scientists have taken advantage of the catalytic power of enzymes. Indeed, many enzymes have been isolated from living organisms and purified for use in the home and in entire industries. In the 1950s, ways were found to induce bacteria to produce commercial quantities of some kinds of enzymes. Since some of the "dirt" on soiled clothes is food stains and related substances, these enzymes were added to various detergent formulations. By the late 1960s, many detergent formulations contained enzymes.

Expensive, high-pressure television advertising led to the widespread use of enzyme detergents. A whole new market was developed for presoak formulations. Washing machines were redesigned so that they included a presoak phase in the washing cycle.

The enzyme boom was rather short-lived. Attacks came on several fronts. Proteolytic enzymes were found to cause hemorrhage in the lungs of laboratory animals. Skin rashes developed,* particularly in the workers who were constantly exposed to the enzymes in the factory. The enzymes were found to contain high concentrations of toxic arsenic. The effect of pouring these enzymes into the waterways was also questioned. Most damning of all, however, was the finding that presoaking in enzyme detergents had little or no demonstrated advantage over presoaking in ordinary detergent formulations. Manufacturers were forced by the Federal Trade Commission to reduce drastically their claims. By 1971, enzyme detergents had largely disappeared from the market, although a few formulations are still available.

Enzymes are also used in the food industry. Meat tenderizers contain *papain*, an enzyme obtained from the milky juice of unripe papayas. Papain is a proteolytic enzyme. It cuts the large protein molecules responsible for toughness down to smaller ones, making the meat more tender. Other proteolytic enzymes help predigest foods for babies. Tough, fibrous protein foods are broken down into "soups" that are more readily digested. Interestingly enough, protein hair conditioners are made in much the same way. Collagen, a by-product of the meat-packing industry, is broken down to a "soup" for the hair.

Enzymes are also used in medicine. One such use is in the treatment of one of several forms of hemophilia. The clotting of blood is a complicated process. (This should not be surprising: it is clear that nature must take some precautions to prevent such clotting while the blood is journeying through the blood vessels.) Many of the preliminary steps in the clotting process involve the conversion of proenzymes to their active forms. We shall detail only the final steps. First, prothrombin must be converted to thrombin. This process itself requires a proteolytic enzyme called Factor X_a (read "factor ten-A").

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*It should not be surprising that proteolytic enzymes attack the skin, because skin is largely protein. Enzymes do seem to be effective in helping to remove protein stains such as those from blood, urine, meat juices, gravies, chocolate, and tea. There is also evidence that the enzymes damage nylon fabrics. Like the proteins, nylons are polyamides. The enzymes should not be used on protein fibers such as silk and wool.

$$\text{Prothrombin} \xrightarrow{\text{Factor } X_a} \text{thrombin}$$

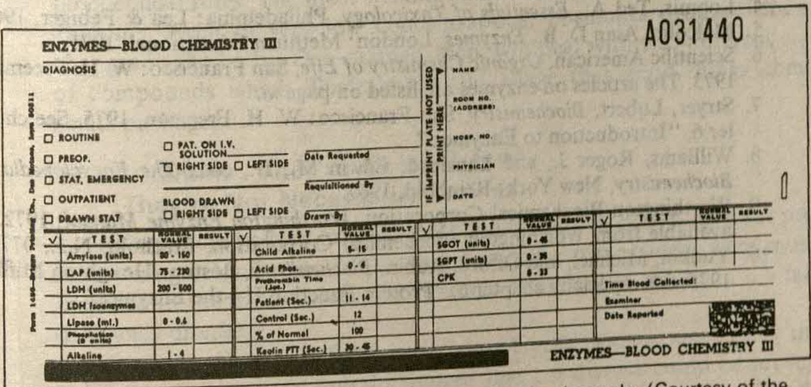
Thrombin, in turn, serves as an enzyme for the conversion of fibrinogen to fibrin.

$$\text{Fibrinogen} \xrightarrow{\text{thrombin}} \text{fibrin}$$

Fibrin is the actual material of the blood clot.

In the form of hemophilia mentioned here, the Factor X_a is missing. The absence of this enzyme is hereditary. It has been found, however, that the venom of a snake called Russell's viper is effective in converting prothrombin to thrombin. This venom has been used as a treatment for some cases of hemophilia.

A far less exotic but far more widespread medical application of enzymes is in the area of diagnosis. Clinical analysis for enzymes in body fluids or tissues is a common diagnostic technique. For example, elevated blood levels of creatine phosphokinase (CPK) and glutamic-oxalacetic transaminase (GOT) accompany some forms of severe heart disease. A blood analysis which shows high levels of CPK may indicate that the heart muscle has suffered serious damage. On the other hand, many forms of strenuous (and healthful) physical activity will also result in elevated CPK levels. The enzyme mediates the reaction which serves as one source of energy for muscle contraction. Indeed, it is even possible for the CPK level to rise simply because someone who hates needles has tensed up while waiting for the blood sample to be taken. Nonetheless, as **figure 26.11** suggests, analysis for spe-



ENZYMES—BLOOD CHEMISTRY III

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DIAGNOSIS

☐ ROUTINE
☐ PREOP.
☐ STAT, EMERGENCY
☐ OUTPATIENT
☐ DRAWN STAT

☐ PAT. ON I.V. SOLUTION
☐ RIGHT SIDE ☐ LEFT SIDE

BLOOD DRAWN
☐ RIGHT SIDE ☐ LEFT SIDE

Date Requested
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NAME
ROOM NO. (ADDRESS)
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✓	TEST	NORMAL VALUE	RESULT	✓	TEST	NORMAL VALUE	RESULT	✓	TEST	NORMAL VALUE	RESULT	✓	TEST	NORMAL VALUE	RESULT
	Amylase (units)	80 - 150			Child Alkaline	5 - 15			SGOT (units)	0 - 45					
	LAP (units)	75 - 230			Acid Phos.	0 - 6			SGPT (units)	0 - 35					
	LDH (units)	200 - 500			Prothrombin Time (Jan.)				CPK	0 - 33					
	LDH Isoenzymes				Patient (Sec.)	11 - 14									
	Lipase (ml.)	0 - 0.6			Control (Sec.)	12									
	Phosphatase (B units)				% of Normal	100									
	Alkaline	1 - 4			Kaolin PTT (Sec.)	30 - 45									

Time Blood Collected:
Examiner
Date Reported

ENZYMES—BLOOD CHEMISTRY III

Form 1490—Briggs Printing Co., Des Moines, Iowa 50311

Figure 26.11 A hospital form for clinical analysis of a blood sample. (Courtesy of the Briggs Corporation, Des Moines, Iowa.)

cific enzymes is considered one valuable source of data on which to base a medical diagnosis.

As we learn more about the structure and function of enzymes, we will no doubt find many more uses for them in industry, foods, and medicine.

Problems

1. Define and, where appropriate, give an example for each of the following.
   - a. enzyme
   - b. substrate
   - c. optimum pH
   - d. optimum temperature
   - e. active site
   - f. allosteric site
   - g. cofactor
   - h. coenzyme
   - i. proenzyme
   - j. feedback inhibition
   - k. apoenzyme
2. List four classes of enzymes and give an example of each.
3. Do enzymes cause reactions to take place? Explain fully.
4. Do enzymes change the *extent* of a reaction? Explain fully.
5. What is the chemical nature of enzymes?
6. What is the lock-and-key model of enzyme action?
7. Enzymes are said to exhibit specificity. Define or illustrate these terms.
   - a. absolute specificity
   - b. stereospecificity
   - c. reaction specificity
   - d. linkage specificity
8. How might each of these inactivate an enzyme?
   - a. heat
   - b. lead ions
   - c. ozone
   - d. too much hydrogen ion
9. Explain the significance of the shape of the curve in **figure 26.5.**
10. How does EDTA work as an antidote for lead poisoning?
11. Why is cyanide a poison?
12. How does thiosulfate act as an antidote for cyanide poisoning?
13. Explain, with examples, the utility of proenzymes.
14. List three commercial uses for enzymes.

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chapter 27

Vitamins and Hormones

Carbohydrates, fats, and proteins are the three major classes of foods. To remain healthy we must take in relatively large amounts of each of these substances. They are not, however, the only nutrients we require. Some of our needs are satisfied only by vitamins and minerals. The minerals, inorganic ions of critical importance to our health, were discussed as a group in chapter 12. Vitamins will be considered in the present chapter.

We normally eat three meals a day to satisfy our need for carbohydrates, fats, and proteins, but all the necessary vitamins can be packed into a single small pill. So small are the required amounts that not even a vitamin pill is necessary. We can get all we need simply by eating a balanced diet. Nature has thoughtfully incorporated minute but adequate amounts of vitamins into our various foodstuffs.

What do hormones have in common with vitamins? Both play critical biochemical roles. The most striking similarity, however, is in their effective amounts. Even in very low concentrations, hormones produce dramatic changes in the body. This chapter, then, will deal with two different classes of compounds which illustrate the old adage that good things come in small packages.

27.1 Vitamins: They're All Vital, but They're Not Necessarily Amines

Vitamins are specific organic compounds that our bodies need for proper functioning. Our bodies can't synthesize these compounds; they must be included in the diet. Absence or shortage of a vitamin results in a vitamin-deficiency disease.

One such disease, called scurvy, had plagued seamen since early times. In 1747, a British navy captain showed that the disease could be prevented by the inclusion of fresh fruit or vegetables in the diet. A convenient fresh fruit to carry on long voyages (they didn't have refrigeration) was the lime.

British ships put to sea with barrels of limes aboard. The sailors ate a lime or two every day and remained free of scurvy. British sailors came to be known as "lime eaters" or simply "limeys."

In 1897, the Dutch scientist Christiaan Eijkman showed that polished rice lacked something found in the hulls of whole-grain rice. Lack of that "something" caused the disease beriberi, which was quite a problem in the Dutch East Indies at that time.

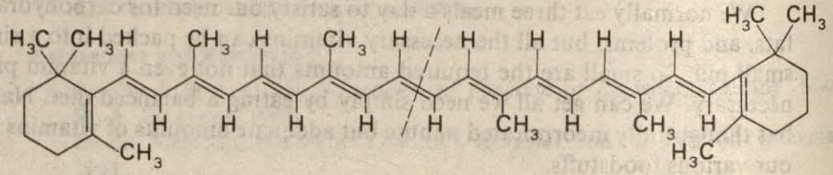
A British scientist, F. G. Hopkins, fed a synthetic diet of carbohydrates, fats, proteins, and minerals to a group of rats. The rats were unable to sustain healthy growth. Again, something was missing.

In 1912, Casimir Funk, a Polish biochemist, coined the word *vitamine* (from the Latin *vita,* "life") for these missing factors. Funk thought that all contained the amino group. The final *-e* was dropped after it was found that not all the factors were amines. The generic term became *vitamin*. Eijkman and Hopkins shared the 1929 Nobel Prize in medicine and physiology for their important discoveries.

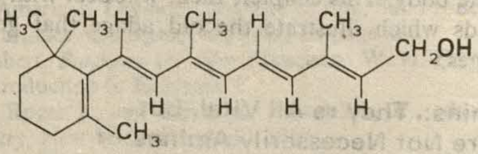
The vitamins are divided into two broad categories, the *fat-soluble* group, including A, D, E, and K, and the *water-soluble* group, made up of the B complex and vitamin C.

27.2 Vitamin A and the Chemistry of Vision

Plants make a class of colored compounds called carotenoid pigments. Four of these can be converted into vitamin A by animals. These are *provitamins*—vitamin precursors. A typical carotenoid pigment, β-carotene, has a number of double bonds, all of which have the *trans* configuration.

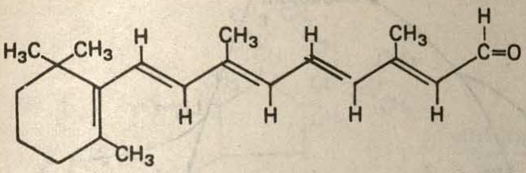

H_3C CH_3 H CH_3 H CH_3 H H H H H H_3C CH_3
H H H H H CH_3 H CH_3 H
CH_3 H_3C

This molecule can be cleaved at the central double bond to give two molecules of vitamin A. Note that vitamin A is an unsaturated alcohol.

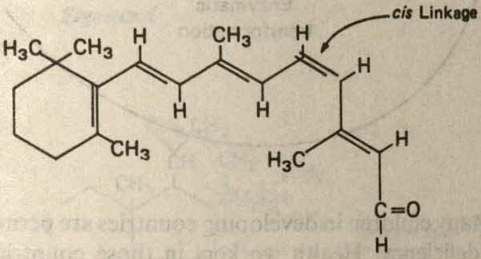


As would be expected from its structure, vitamin A is insoluble in water but soluble in fats and fat solvents. The pure compound is a crystalline solid which melts at 64 °C.

The relationship between vitamin A and vision has been worked out in considerable detail. In the body, some vitamin A is isomerized and oxidized. The isomerization converts the all-*trans* compound to a molecule in which one of the double bonds has a *cis* arrangement. The oxidation converts the



All-trans-*retinal*



11-cis-*Retinal*

Figure 27.1 Retinal isomers.

alcohol group to an aldehyde group. The product which results is called 11-*cis*-retinal (**figure 27.1**).

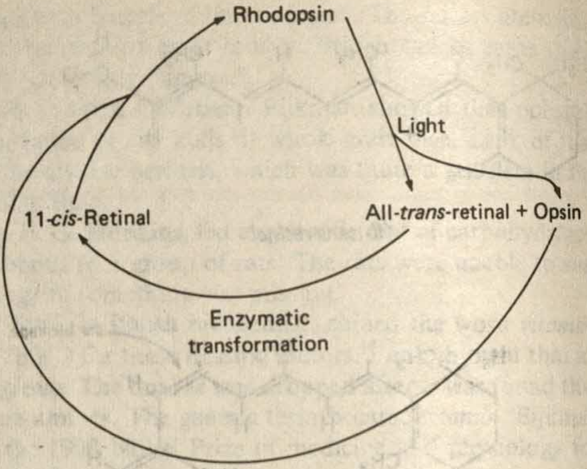
The retina of the human eye contains two kinds of receptor cells, rods and cones. 11-*cis*-Retinal forms a complex with various proteins, and these complexes are the photosensitive chemicals found in the rods and cones. Rhodopsin, a complex of 11-*cis*-retinal and a protein called opsin, is the visual pigment found in the cones. When light strikes rhodopsin, 11-*cis*-retinal is isomerized to the all-*trans* isomer (**figure 27.1**). This change in structure is accompanied by a change in electrical potential. The photoisomerization of the retinal triggers a nerve impulse—we see. The rhodopsin complex then splits into opsin and the free aldehyde. The all-*trans* retinal is converted by enzymes back to 11-*cis*-retinal, which again complexes opsin, completing the visual cycle (**figure 27.2**). Some retinal is lost during the regeneration of rhodopsin. It must be replaced by vitamin A from the bloodstream.

It is interesting to note that, of all the tissues in the body, the retina has the highest respiration rate. You may think of seeing as a rather passive activity, but vision is metabolically demanding.

The role of vitamin A in vision is something we understand fairly well. In addition, we also know that a deficiency of this vitamin affects most of the body's organs. What we do not know is the detailed biochemistry of vitamin A as it relates to all these other organs. We can, however, describe some of the effects of vitamin A deficiency.

Vitamin A is required for normal growth. Young animals fed a diet lacking in the vitamin simply fail to grow. One of the earliest manifestations of vitamin A deficiency is a loss of night vision (a function of the rod cells in the retina). Mucous membranes may harden, dry, and crack. In cases of severe deprivation, victims may exhibit xerophthalmia, a condition characterized by inflammation of the eyes and eyelids, leading ultimately to in-

Figure 27.2 A schematic diagram of the visual cycle.



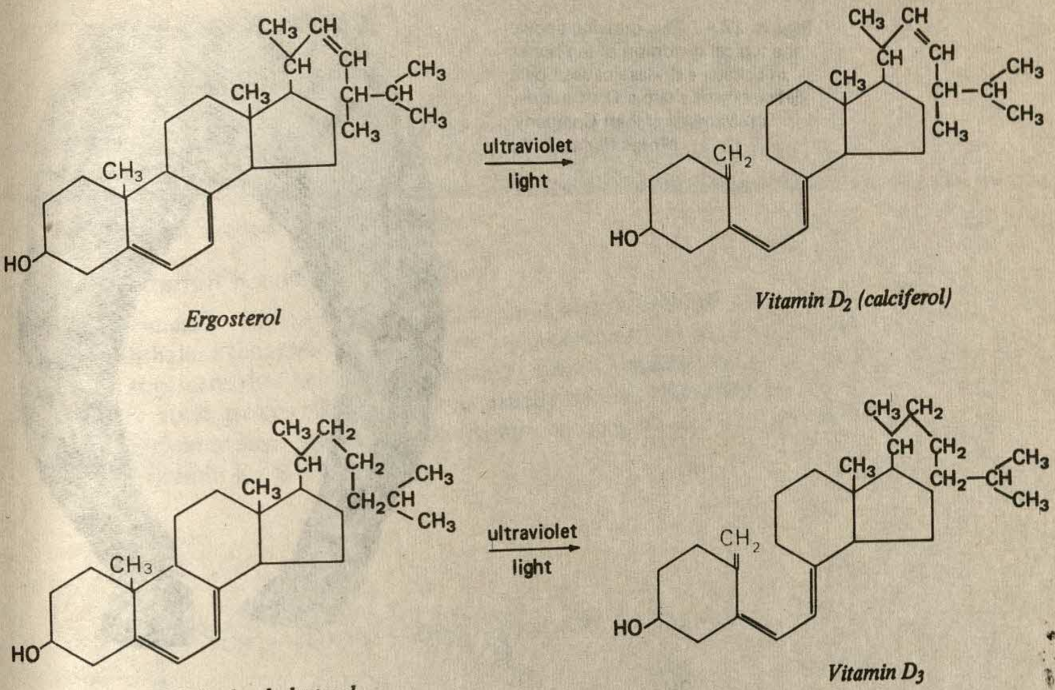
fection and blindness. Many children in developing countries are permanently blinded by vitamin A deficiency. Health workers in those countries often carry injectible solutions of the vitamin for emergency treatment of such cases. Vitamin A (an alcohol) can be stored as an ester in the liver. Adults, while on an adequate diet, can store several years' supply in this form. Small children, without such reserves, are particularly susceptible to vitamin A deprivation.

Vitamin A is found in high concentration in fish liver oils. Liver, eggs, fish, butter, and cheese are also good sources. The provitamin forms are found in carrots, tomatoes, and green vegetables. If taken in excess, the vitamin is stored rather than excreted. Large excesses cause irritability, dry skin, and a feeling of pressure inside the head. Massive doses of vitamin A administered to pregnant rats result in malformed offspring. The ready availability of large dosage forms and the pill-popping propensity of much of the population led the U.S. Food and Drug Administration in 1973 to limit the amount of vitamins A and D in nonprescription capsules.

27.3 Vitamin D: Sunlight and Bones

There are several chemical compounds that have vitamin D activity. Only two commonly occur in foods or are used in drugs and food supplements. Each is formed from a precursor by the action of ultraviolet light (**figure 27.3**). Vitamin D_2 (calciferol) is synthesized by irradiation of ergosterol, a compound found in yeast and other molds. Vitamin D_3 is formed in the skin of animals by the action of sunlight on 7-dehydrocholesterol. The two vitamins differ only in the structure of their side chains; D_2 contains an extra carbon and a double bond. (There is no vitamin D_1. The material which was originally given this designation proved to be a mixture of compounds which included calciferol.)

Vitamin D increases the utilization of calcium and phosphorus by the body. Deficiency in infants and growing children results in abnormal bone formation, a condition known as *rickets*. The condition is characterized by



Ergosterol

Vitamin D_2 (calciferol)

7-Dehydrocholesterol

Vitamin D_3

Figure 27.3 Formation of two forms of vitamin D by action of ultraviolet light on corresponding provitamins.

bowed legs, knobby bone growths where the ribs join the breastbone (called a "rachitic rosary"), pigeon breast, and poor tooth development. In adults, with completed bone growth, rickets does not develop. Women may develop osteomalacia, a condition characterized by fragile bone structure, if deficient in vitamin D. This condition is rare but may occur after several pregnancies.

The fish liver oils are a good source of vitamin D as well as of vitamin A. Irradiated ergosterol is added to milk as a supplemental source. Vitamin D is the "sunshine vitamin." Children who are outside a lot seldom suffer a deficiency, for sunlight converts 7-dehydrocholesterol in the skin to vitamin D.

Vitamin D, like vitamin A, is fat soluble. Amounts taken in excess are stored in body fat. The effects of large overdoses are even more severe than with vitamin A. Too much vitamin D can cause pain in the bones, nausea, diarrhea, and weight loss. Bonelike material may be deposited in kidney tubules, in blood vessels, and in heart, stomach, and lung tissue. Like vitamin A, amounts of vitamin D in nonprescription capsules are regulated by the FDA.

27.4 Vitamin E: Sex and Aging Cells

As was true for vitamin D, there are several compounds with vitamin E activity. The compounds are called tocopherols; the most potent of these is α-tocopherol.

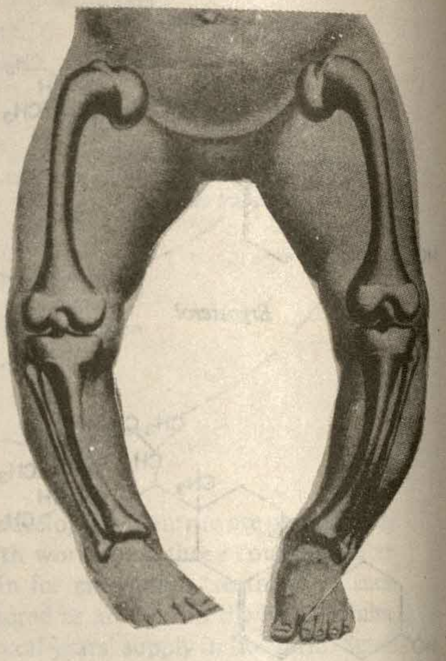


Figure 27.4 This drawing shows the typical distortion of leg bones in rickets, a disease caused by a deficiency of vitamin D. (Courtesy of Warner-Lambert Company, Morris Plains, N.J.)

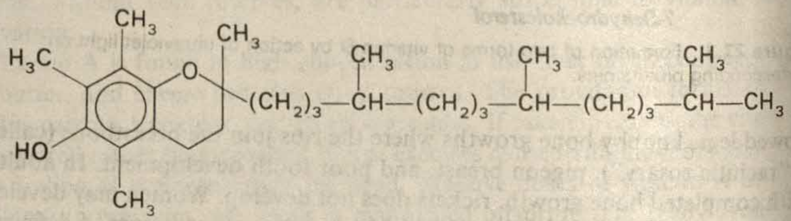


Figure 27.5 Too much vitamin D causes the deposit of bonelike material in joints. (Courtesy of Marc Moldawer, Texas Medical Center, Houston.)

The tocopherols are phenols. Many phenols are antioxidants; they protect other compounds from being oxidized by reacting themselves with the oxidizing agent (oxygen in the atmosphere, for example). Vitamin E exhibits similar properties.

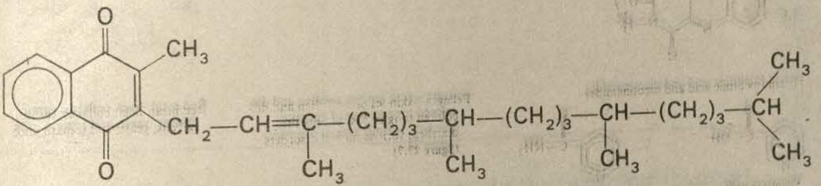
Rats deprived of vitamin E develop a scaly skin, muscular weakness, and sterility. Vitamin E deficiency can also lead to vitamin A deficiency. Vitamin A can be oxidized to a nonactive form when vitamin E is no longer present to act as an antioxidant. Indeed, the loss of vitamin E's antioxidant effect is believed to be responsible for all of the symptoms of vitamin E deficiency. Polyunsaturated fatty acids, especially, are oxidized at increased rates. The muscular dystrophy, sterility, and other symptoms manifested by animals deficient in vitamin E are believed to result from this "simple" change in body chemistry.

Because of its effect on fertility, vitamin E is called the antisterility vitamin. Some food faddists promote the ingestion of large amounts of vitamin E to increase sexual prowess, combat wrinkled skin, and prevent heart attacks. There is no unambiguous evidence for any of these claims. However, Lester Packer and James R. Smith, of the University of California at Berkeley, have shown that vitamin E slows the aging of cultured human cells. Just how this might be extrapolated to the entire human organism is not clear.

Vitamin E is available in wheat germ oil, green vegetables, vegetable oils, egg yolk, and meat. Most nutritionists contend that it would be nearly impossible to eat a diet deficient in vitamin E. Like vitamins A and D, vitamin E is fat soluble and thus is stored in the body. Large doses may waste money, but they do not seem to cause harmful effects as do vitamins A and D. A belief in the efficacy of vitamin E, however, may lead to the dangerous postponement of needed medical treatment.

27.5 Vitamin K and Blood Clotting

Chemically, vitamin K has a fused ring system related to the structure of naphthalene (chapter 14). One of the rings contains two carbonyl groups, an arrangement that has the special name *quinone*. Attached to the quinone ring are alkyl groups. One of these is usually methyl. The other has 20 or more carbon atoms. Many compounds have vitamin K activity. The structure of vitamin K_1 is given here.



Vitamin K, like vitamins A, D, and E, is insoluble in water but soluble in fats and fat solvents. Vitamin K is necessary for the formation of prothrombin (chapter 26), one of the enzyme precursors involved in blood clotting. Deficiency will increase the time required for clotting of the blood. Symptoms are bleeding under the skin and in muscles, leading to ugly "bruises" from what would otherwise be minor blows. Infants lacking in vitamin K may die from hemorrhaging in the brain. Increased vitamin K intake by pregnant women has lowered the incidence of this disease in newborn infants. Good sources of vitamin K are spinach and other green leafy vegetables. Synthetic compounds with K activity are readily available.

27.6 The B Complex . . . And Complex It Is

In chapter 26 we saw that some enzymes require cofactors, nonprotein components, for proper function. Organic cofactors are called coenzymes, and many coenzymes are vitamin B derivatives.

There is really no vitamin B. What was once called vitamin B has long since been recognized as a complicated mixture of factors. The term *B complex* is now used to designate a group of water-soluble vitamins found together in many food sources. **Table 27.1** lists the members of the B complex, their structures and sources, and the diseases associated with their deficiencies.

The B complex vitamins are water soluble. The body has a very limited capacity to store water-soluble vitamins. It will excrete anything over the amount that it can immediately use. Thus, water-soluble vitamins must be taken in at frequent intervals, whereas a single large dose of a fat-soluble vitamin can be used by the body over a period of several weeks.

The structures of the B complex members (**table 27.1**) range from the relatively simple one of niacin to the very complex one of B_{12}. Each of the B vitamins is incorporated in coenzyme molecules. In some instances, the

Table 27.1
Members of the B complex of vitamins

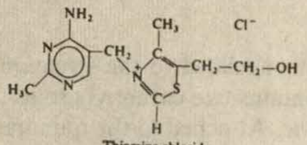
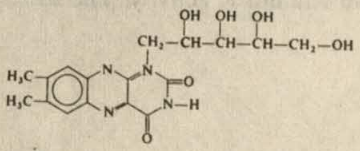
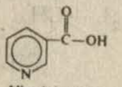
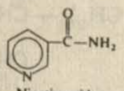
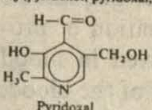
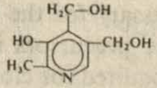
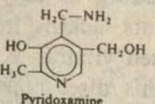
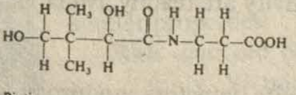
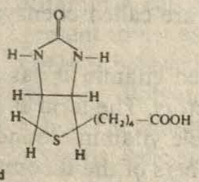
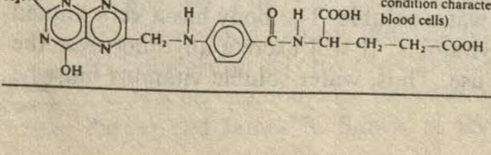
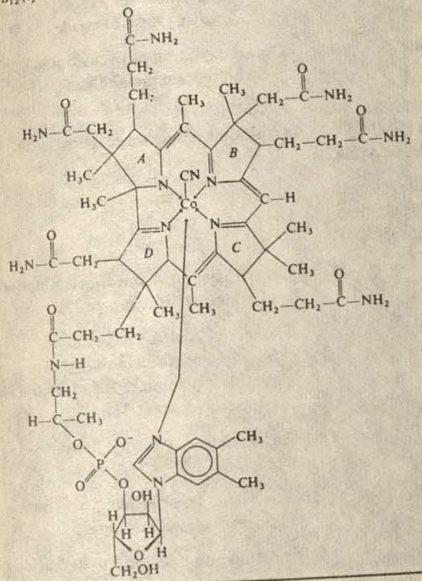
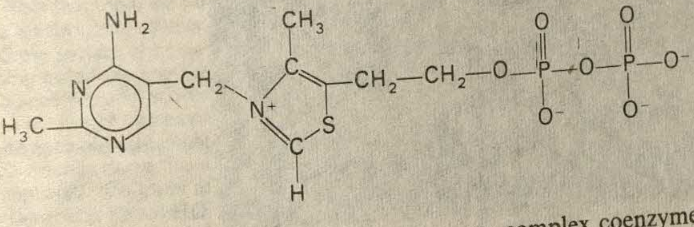
Name and Structure	*Deficiency Symptoms*	*Sources*
B_1 (thiamine)  **Thiamine chloride**	Beriberi—polyneuritis resulting in muscle paralysis, enlargement of heart, and ultimately heart failure	Germ of cereal grains, legumes, nuts, milk, and brewers yeast
B_2 (riboflavin) 	Dermatitis, glossitis (tongue inflammation)	Milk, red meat, liver, egg white, green vegetables, whole wheat flour (or fortified white flour), and fish
Niacin (nicotinic acid and nicotinamide)  **Nicotinic acid**  **Nicotinamide**	Pellagra—skin lesions, swollen and discolored tongue, loss of appetite, diarrhea, various mental disorders (**figure 27.7**)	Red meat, liver, collards, turnip greens, yeast, and tomato juice
B_6 (pyridoxol, pyridoxal, and pyridoxamine)  **Pyridoxal**  **Pyridoxol (pyridoxine)**  **Pyridoxamine**	Dermatitis, apathy, irritability, and increased susceptibility to infections; convulsions in infants	Eggs, liver, yeast, peas, beans, and milk
Pantothenic acid  $HO-\underset{H}{\overset{H}{C}}-\underset{CH_3}{\overset{CH_3}{C}}-\underset{H}{\overset{OH}{C}}-\overset{O}{\overset{\|}{C}}-\overset{H}{N}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-COOH$	(Possibly) emotional problems and gastrointestinal disturbances	Liver, eggs, yeast, and milk
Biotin 	Dermatitis	Beef liver, yeast, peanuts, chocolate, and eggs (although this vitamin cannot be synthesized by humans, it is a product of their intestinal bacteria)
Folic acid 	Anemias (folic acid is used in the treatment of megaloblastic anemia, a condition characterized by giant red blood cells)	Liver, kidney, mushroom, yeast, and green leafy vegetables

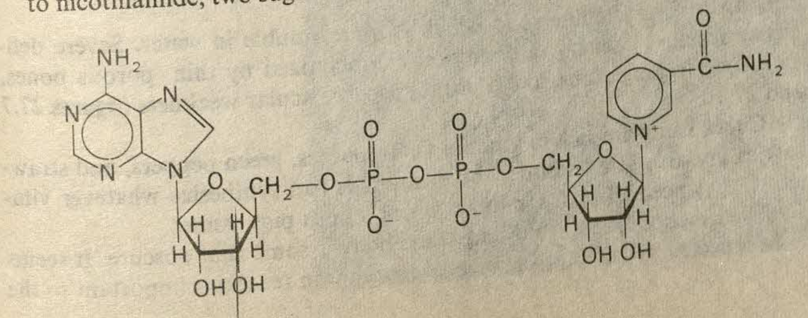
Table 27.1 (continued)

Name and Structure	*Deficiency Symptoms*	*Sources*
B_{12} (cyanocobalamine) 	Pernicious anemia	Liver, meat, eggs, and fish (not found in plants)

coenzymes are simple derivatives of the vitamins. In the coenzyme thiamine pyrophosphate, for example, the primary alcohol group of thiamine (**table 27.1**) is esterified with pyrophosphoric acid.



In contrast, nicotinamide is part of a much more complex coenzyme. The coenzyme, nicotinamide adenine dinucleotide (NAD^+), contains, in addition to nicotinamide, two sugar units, a pyrophosphate group, and a purine base.



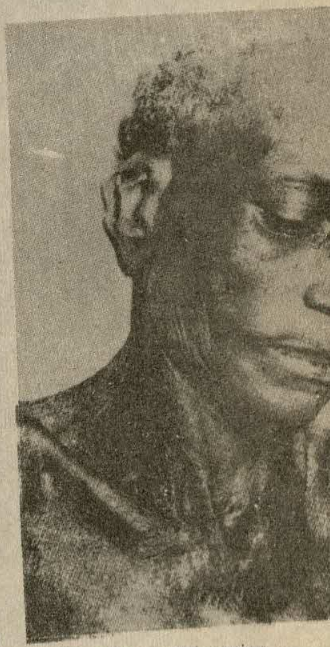


Figure 27.6 Inflammation and abnormal pigmentation characterize pellagra, caused by niacin deficiency. (Courtesy of the World Health Organization, New York.)

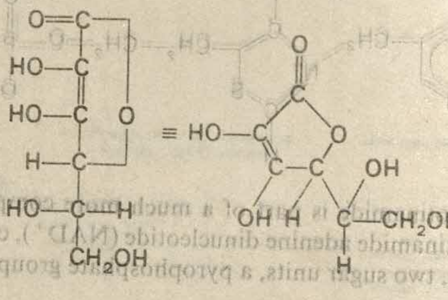
Table 27.2
The B complex coenzymes

Vitamin	Name of Coenzyme	Some Biochemical Processes Involving the Coenzyme
B_1 (thiamine)	Thiamine pyrophosphate	Decarboxylation of pyruvic acid during carbohydrate metabolism (chapter 30)
B_2 (riboflavin)	Flavin mononucleotide (FMN), flavin adenine dinucleotide (FAD)	Oxidation-reduction reactions
Niacin	Nicotinamide adenine dinucleotide (NAD^+), nicotinamide adenine dinucleotide phosphate ($NADP^+$)	Oxidation-reduction reactions
B_6 (pyridoxine group)	Pyridoxal phosphate	Decarboxylations and transamination of amino acids (chapter 32)
Pantothenic acid	Coenzyme A (CoA)	Transfer of acetyl, succinyl, and benzoyl groups in carbohydrate synthesis (chapter 30) and lipid synthesis (chapter 31)
Biotin	Biotin	Carboxylation-decarboxylation reactions
Folic acid	Tetrahydrofolic acid (FH_4) and derivatives	One-carbon transfer reactions (purine and amino acid syntheses)
B_{12} (cyanocobalamine)	Cobamide coenzymes	Isomerization reactions, dehydrations, and methyl group biosynthesis

The names and some functions of the B complex coenzymes are listed in **table 27.2.**

27.7 Vitamin C, Scurvy, Linus Pauling, and The Common Cold

Chemically, vitamin C is ascorbic acid.



It is a white, crystalline solid which is quite soluble in water. Severe deficiency results in scurvy, a condition characterized by thin, porous bones, sore and bleeding gums, and a pronounced muscular weakness (**figures 27.7** and **27.8**).

Citrus fruits are rich in vitamin C. Tomatoes, green peppers, and strawberries are also good sources. Most animals can synthesize whatever vitamin C they need. Humans, monkeys, and guinea pigs cannot.

The function of ascorbic acid in the body is somewhat obscure. It seems to be a necessary cofactor in some hydroxylation reactions important to the

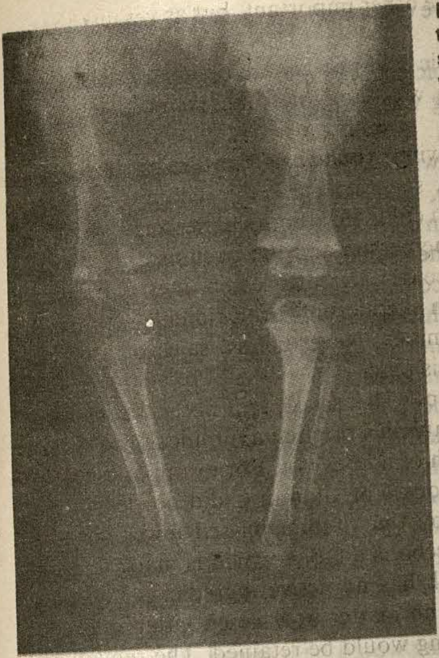


Figure 27.7 An X-ray photograph of the legs of a patient with infantile scurvy, caused by a deficiency of vitamin C. (Reprinted with permission from Arnow, L. Earle, *Introduction to Physiological and Pathological Chemistry*, 9th ed., St. Louis: C. V. Mosby, 1976. Copyright © 1976, 1972, 1966, 1961, 1957, 1953, 1949, 1943, 1939 by C. V. Mosby Company.)

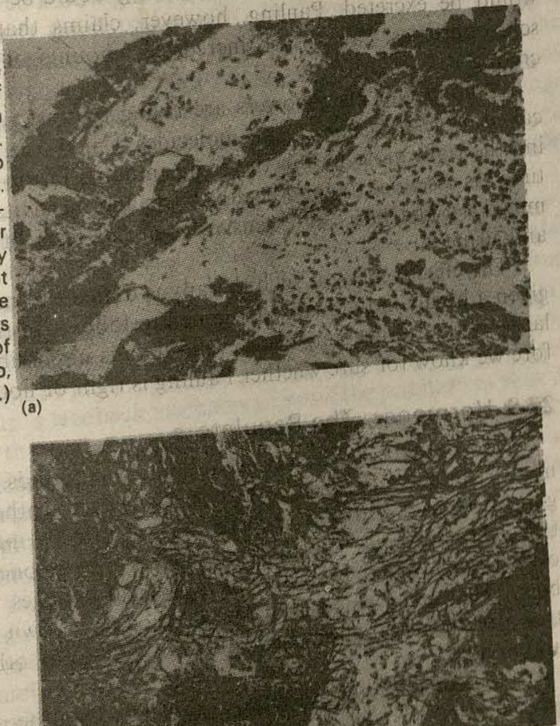


Figure 27.8 The effect of ascorbic acid on bone formation. (a) Cross section of bone-forming cells from a guinea pig dying of scurvy. Note that there are no connective tissue fibers. (b) Cross section of bone-forming cells from another guinea pig with scurvy after 72 hours of treatment with ascorbic acid. Note that connective tissue fibers have appeared. (Courtesy of Upjohn Company, Kalamazoo, Mich.)

synthesis of collagen. It may also have other important, but as yet unknown, functions.

Only about 40 to 75 mg of ascorbic acid per day are necessary to prevent scurvy. Daily intake of over 100 mg was thought to be excreted and thus wasted.

In 1970, though, Linus Pauling, winner of two Nobel Prizes (for chemistry in 1954 and for peace in 1962), suggested that this vitamin could be used as a weapon against the common cold. He recommended daily dosages of 250 to 15 000 mg, depending on the person and the circumstances. Vitamin C, he said, could either prevent colds or greatly lessen their symptoms.

Pauling's claims were greeted with skepticism—even ridicule—by many in the scientific and medical communities. Nevertheless, sales of ascorbic acid zoomed as people rushed to try his plan.

Figure 27.9 Linus Pauling advocates massive doses of vitamin C as a preventive of the common cold. (Photo by Margo Moore.)

Who was right, Pauling or his critics? The issue is still not settled. Much research has been undertaken since Pauling's original announcement. Some of it seems to confirm his claims; much of it does not. For example, a recent Canadian study showed that massive doses of vitamin C did not lessen the incidence of colds per se, but those on the vitamin missed fewer days of work than those on a placebo. (A placebo is a tablet which is made to look and taste like the real thing but which has no active ingredients.) Studies reported in August 1973 showed that no matter how much vitamin C one swallowed, a maximum of about 200 mg would be retained. The remainder would be excreted. Pauling, however, claims that some people, notably schizophrenics, can absorb incredible amounts of vitamin C without excreting it.

Pauling and his followers are trying to start a new kind of medicine, called *orthomolecular* ("right molecules") medicine. He believes that "having the right molecules in the right amounts in the right place at the right time" is essential to good health. Diets and megavitamin dosages are determined on the basis of extensive chemical tests of an individual's blood and urine.

The effectiveness of such therapy is difficult to measure. Each patient is given a highly individualized regimen to follow. Testing such procedures on large groups to get statistically valid data is impossible. It may be years before we know for sure whether Pauling is right or not.

27.8 Hormones: The Regulators

Like vitamins, hormones are organic compounds. Unlike vitamins, hormones can be synthesized in the body. They are synthesized in the endocrine glands (**figure 27.10**) and then discharged directly into the circulatory system. They serve as "chemical messengers." Hormones released in one part of the body signal profound physiological changes in other parts of the body. They cause reactions to speed up or slow down. In this way they control growth, metabolism, reproduction, and many other functions of body and mind.

If we consider hormones as messengers, then the pituitary gland (hypophysis) must be viewed as the central dispatcher or control. Many of the pituitary hormones control the production of hormones by other endocrine

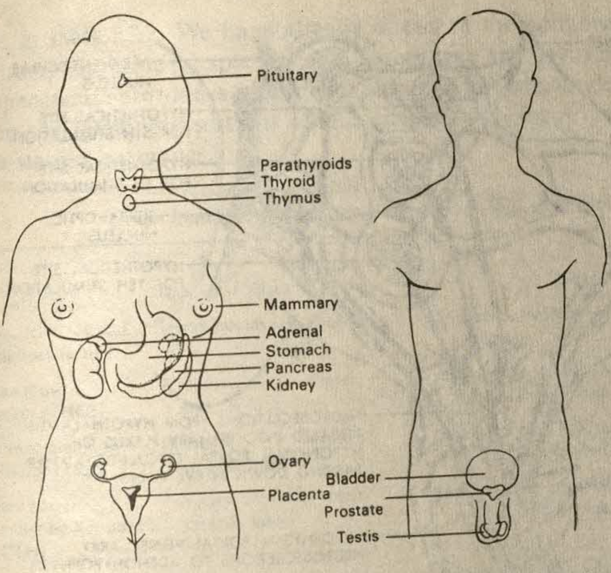


Figure 27.10 The approximate location of endocrine glands in the human body.

glands. The removal of portions of the pituitary gland results in atrophy of other endocrine glands. Shut down the central control and you ultimately shut down much of the endocrine system. The pituitary itself responds to hormone signals from the hypothalamus. The hypothalamus secretes hormones, called releasing factors, which trigger the production of the pituitary hormones. The hypothalamus is triggered by nerve impulses. The sequence is this. A nerve impulse signals the hypothalamus, the hypothalamus signals the pituitary, the pituitary signals some target endocrine gland, the gland signals some target tissue, and the tissue responds in a specific way (**figure 27.11**).

Let us take just a moment to consider the extraordinary complexity of this system. For example, in response to neural stimulation, the hypothalamus produces thyrotropin-releasing factor (TRF). The TRF reaches the pituitary and causes that gland to produce thyroid-stimulating hormone (TSH). In the presence of TSH, the thyroid gland releases the hormone thyroxine. Thyroxine signals the cells to increase their metabolic rate. As the level of thyroxine builds up, a feedback mechanism causes the pituitary to slow down its production of thyroid-stimulating hormone. This, in turn, slows the production of thyroxine by the thyroid, which results in a slowing of the metabolic rate, which gets us back to where we started. The cycle includes the synthesis of proteins and peptides (through the complex process described in chapter 25). It includes the multistep synthesis of the amino acid thyroxine and, ultimately, the speeding up of that complicated combination of reactions we lump together under the heading *metabolism*.

In a healthy individual all of this happens routinely, in perfect balance, and with no conscious direction. And that's just one of the myriad, interrelated biochemical processes which life requires. That it all works, and works so well, is nothing short of miraculous.

Many important human hormones and their physiological effects are

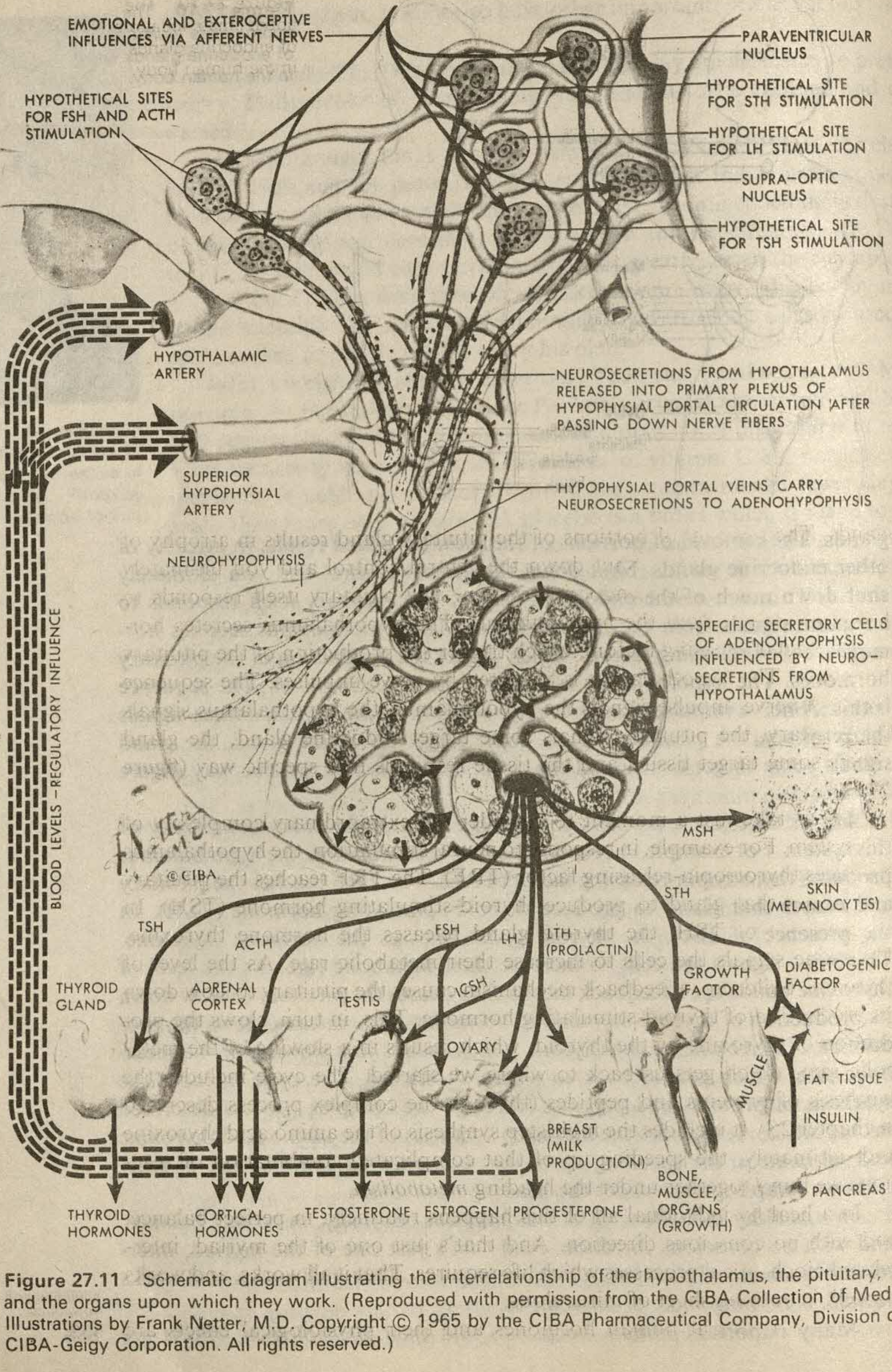

EMOTIONAL AND EXTEROCEPTIVE INFLUENCES VIA AFFERENT NERVES
HYPOTHETICAL SITES FOR FSH AND ACTH STIMULATION
PARAVENTRICULAR NUCLEUS
HYPOTHETICAL SITE FOR STH STIMULATION
HYPOTHETICAL SITE FOR LH STIMULATION
SUPRA-OPTIC NUCLEUS
HYPOTHETICAL SITE FOR TSH STIMULATION
HYPOTHALAMIC ARTERY
NEUROSECRETIONS FROM HYPOTHALAMUS RELEASED INTO PRIMARY PLEXUS OF HYPOPHYSIAL PORTAL CIRCULATION AFTER PASSING DOWN NERVE FIBERS
SUPERIOR HYPOPHYSIAL ARTERY
HYPOPHYSIAL PORTAL VEINS CARRY NEUROSECRETIONS TO ADENOHYPOPHYSIS
NEUROHYPOPHYSIS
SPECIFIC SECRETORY CELLS OF ADENOHYPOPHYSIS INFLUENCED BY NEURO-SECRETIONS FROM HYPOTHALAMUS
BLOOD LEVELS-REGULATORY INFLUENCE
MSH
F. Netter M.D.
© CIBA
STH
SKIN (MELANOCYTES)
TSH
ACTH
FSH
LH
LTH (PROLACTIN)
GROWTH FACTOR
DIABETOGENIC FACTOR
THYROID GLAND
ADRENAL CORTEX
TESTIS
ICSH
OVARY
MUSCLE
FAT TISSUE
INSULIN
BREAST (MILK PRODUCTION)
BONE, MUSCLE, ORGANS (GROWTH)
PANCREAS
THYROID HORMONES
CORTICAL HORMONES
TESTOSTERONE
ESTROGEN
PROGESTERONE

Figure 27.11 Schematic diagram illustrating the interrelationship of the hypothalamus, the pituitary, and the organs upon which they work. (Reproduced with permission from the CIBA Collection of Medical Illustrations by Frank Netter, M.D. Copyright © 1965 by the CIBA Pharmaceutical Company, Division of CIBA-Geigy Corporation. All rights reserved.)

listed in **table 27.3**. We have already discussed the hormones epinephrine and norepinephrine (chapter 19) and vasopressin and oxytocin (chapter 24). The pancreatic hormones insulin and glucagon will be considered in chapter 30. In the remaining sections of this chapter we'll focus our attention on some steroid hormones.

Table 27.3

Some human hormones and their physiological effects

Name	*Gland and Tissue*	*Chemical Nature*	*Effect*
Various releasing and inhibitory factors	Hypothalamus	Peptide	Triggers or inhibits release of pituitary hormones
Human growth hormone (HGH)	Pituitary, anterior lobe	Protein	Controls the general body growth; controls bone growth
Thyroid-stimulating hormone (TSH)	Pituitary, anterior lobe	Protein	Stimulates growth of the thyroid gland and production of thyroxin
Adrenal cortex–stimulating hormone (ACTH)	Pituitary, anterior lobe	Protein	Stimulates growth of the adrenal cortex and production of cortical hormones
Follicle-stimulating hormone (FSH)	Pituitary, anterior lobe	Protein	Stimulates growth of follicles in ovaries of females, sperm cells in testes of males
Luteinizing hormone (LH)	Pituitary, anterior lobe	Protein	Controls production and release of estrogens and progesterone from ovaries, testosterone from testes
Prolactin	Pituitary, anterior lobe	Protein	Maintains the production of estrogens and progesterone, stimulates the formation of milk
Vasopressin	Pituitary, posterior lobe	Protein	Stimulates contractions of smooth muscle; regulates water uptake by the kidneys
Oxytocin	Pituitary, posterior lobe	Protein	Stimulates contraction of the smooth muscle of the uterus; stimulates secretion of milk
Parathyroid	Parathyroid	Protein	Controls the metabolism of phosphorus and calcium
Thyroxin	Thyroid	Amino acid derivative	Increases rate of cellular metabolism
Insulin	Pancreas, beta cells	Protein	Increases cell usage of glucose; increases glycogen storage
Glucagon	Pancreas, alpha cells	Protein	Stimulates conversion of liver glycogen to glucose
Cortisol	Adrenal gland, cortex	Steroid	Stimulates conversion of proteins to carbohydrates
Aldosterone	Adrenal gland, cortex	Steroid	Regulates salt metabolism; stimulates kidneys to retain Na^+ and excrete K^+
Epinephrine (adrenalin)	Adrenal gland, medulla	Amino acid derivative	Stimulates a variety of mechanisms to prepare the body for emergency action including the conversion of glycogen to glucose
Norepinephrine (noradrenalin)	Adrenal gland, medulla	Amino acid derivative	Stimulates sympathetic nervous system; constricts blood vessels, stimulates other glands

Table 27.3 (continued)

Name	*Gland and Tissue*	*Chemical Nature*	*Effect*
Estradiol	Ovary, follicle	Steroid	Stimulates female sex characteristics; regulates changes during menstrual cycle
Progesterone	Ovary, corpus luteum	Steroid	Regulates menstrual cycle; maintains pregnancy
Testosterone	Testis	Steroid	Stimulates and maintains male sex characteristics

27.9 Cortisone: An Adrenocortical Hormone

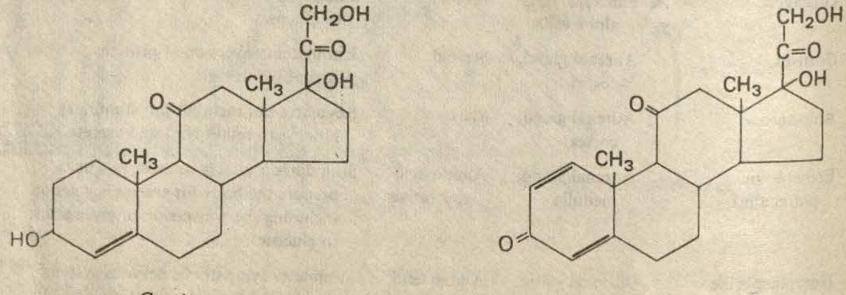
The hormone cortisone is a steroid produced in the outer layer, or cortex, of the adrenal gland. Cortisone is involved in carbohydrate metabolism (chapter 30). It is also used as a medicine. Applied topically or injected, cortisone acts to reduce inflammation. It was once widely used in the treatment of arthritis, but relief was transitory and repeated application caused serious side effects, including the disturbance of the delicately balanced endocrine system. Cortisone has been largely replaced by the related compound prednisone. The latter is effective in much smaller doses; thus side effects are greatly reduced. Structures of cortisone and prednisone are shown in **figure 27.12.**

27.10 Some Sexy Steroids

Closely related in structure to cortisone and prednisone are the sex hormones. It is interesting to note that male sex hormones differ only slightly in structure from female hormones. In fact, the female hormone progesterone can be converted by a simple biochemical reaction into the male hormone testosterone. The physiological action of these structurally similar compounds is obviously markedly different.

Male sex hormones are called *androgens.* They are secreted by the testes. These hormones are responsible for development of the sex organs and for secondary sex characteristics such as the pitch of the voice and hair distribution.

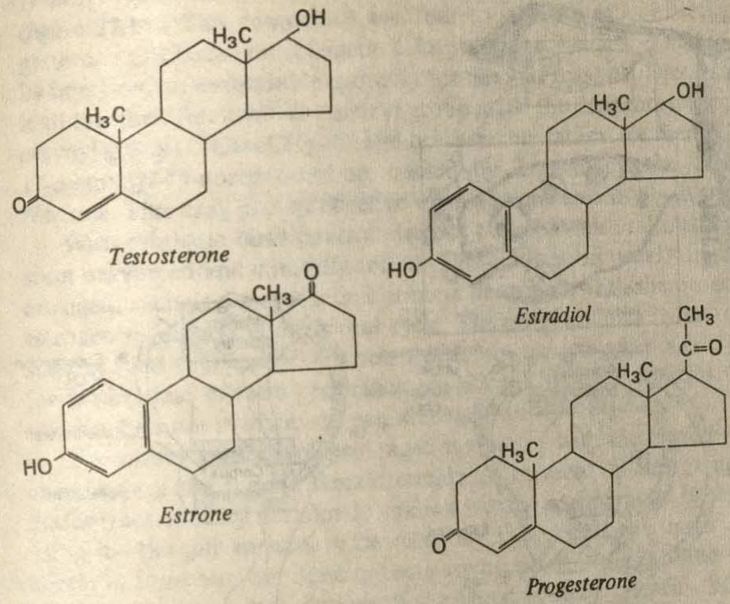
The female sex hormones, called *estrogens,* are produced mainly in the



Cortisone

Prednisone

Figure 27.12 Cortisone and prednisone.


Testosterone

Estradiol

Estrone

Progesterone

Figure 27.13 Some important sex hormones.

ovaries. They control the female sexual functions, such as the menstrual cycle (**figure 27.14**) and the development of breasts and other secondary sexual characteristics. Two important estrogens are estradiol and estrone.

Another important hormone produced in the ovaries is progesterone. It prepares the uterus for pregnancy and also prevents the further release of eggs from the ovaries during pregnancy.

Sex hormones—both natural and synthetic—are sometimes used therapeutically. For example, a woman who has had her ovaries removed may be given female hormones to compensate for those no longer produced by the ovaries. Some of the earliest chemical compounds employed in cancer chemotherapy were sex hormones. The male hormone testosterone was used to treat carcinoma of the breast in females; estrogens, female sex hormones, were given to males to treat carcinoma of the prostate. Sex hormones are also important in sex change operations. After corrective surgery, hormones are administered to promote the development of the proper secondary sexual characteristics.

27.11 Chemistry and Social Revolution: The Pill

When administered by injection, progesterone serves as an effective birth control drug. This knowledge led to attempts by chemists to design a contraceptive which would be effective when taken orally.

The structure of progesterone was determined in 1934 by Adolf Butenandt. Just 4 years later, Hans Inhoffen synthesized the first effective oral contraceptive, ethisterone. Ethisterone had to be taken in large doses to be effective. It never became important as an oral contraceptive.

The next breakthrough came in 1951 when Carl Djerassi synthesized

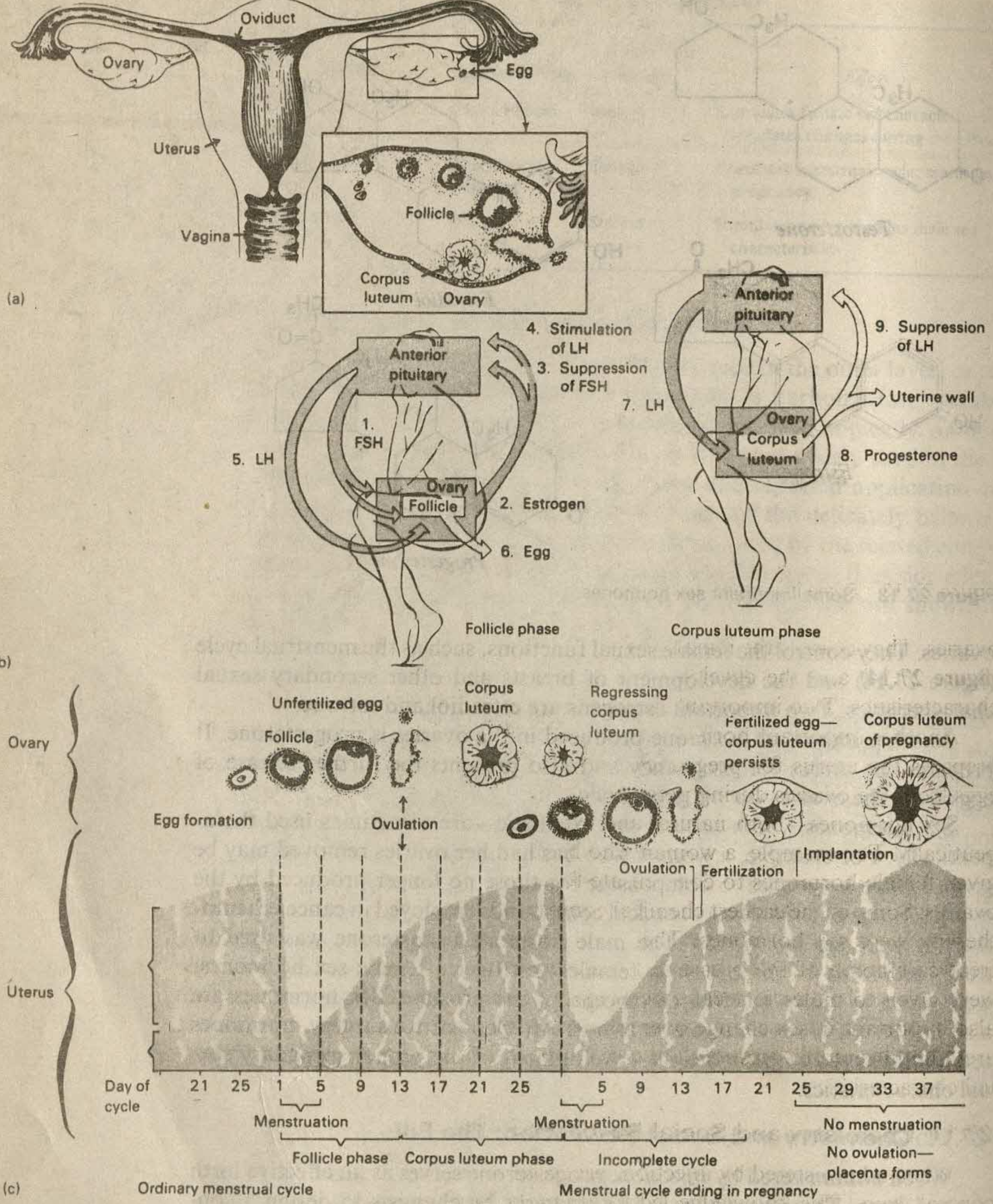


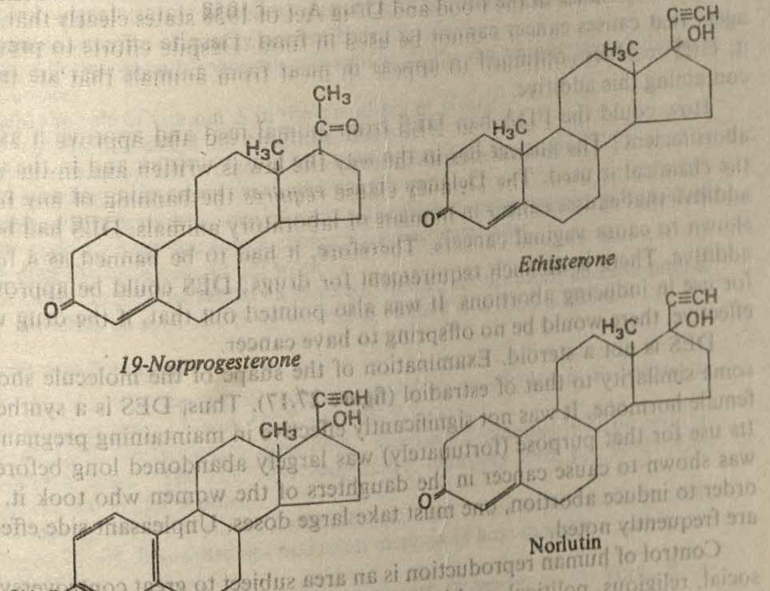
Figure 27.14 The menstrual cycle is controlled by hormones. This illustration shows the normal menstrual cycle. Pregnancy—or the pseudo-pregnancy caused by the pill—prevents ovulation. (a) The female reproductive system. (b) Hormonal control of the female menstrual cycle. (c) Changes in the ovary and uterus. (Adapted with permission from Sparks, Philip D., Nord, Richard P., Unbehaun, Laraine M., Weeks, Thomas F., and Hughes, Eileen G., *Student Study Guide for the Biological Sciences*, 3rd ed., Minneapolis: Burgess, 1973.)

19-norprogesterone, progesterone with one of its methyl groups missing (**figure 27.16**). This compound was four to eight times as effective as progesterone as a birth control agent. Like progesterone itself, it had to be given by injection, an undesirable property for obvious reasons. Djerassi then put it all together. Removal of a methyl group made the drug more effective. The ethynyl group (—C≡CH) allowed oral administration. He then synthesized 17-α-ethynyl-19-nortestosterone, mercifully known by the trade name *Norlutin*. This drug proved effective when administered orally in small doses.

With synthetic birth control steroids available, an oral medication was soon developed and clinically tested. This medication usually combined an estrogen, such as the synthetic hormone mestranol, with the progestin. The estrogen regulates the menstrual cycle. The progestin acts by establishing a state of false pregnancy. A woman does not ovulate when she is pregnant (or in the state of false pregnancy established by the progestin). Since the woman does not ovulate, she cannot conceive.

The ultimate effects of prolonged tampering with the reproductive biochemistry of the human female remain to be seen. In use in the United States since 1960 by perhaps 15 million women—with about 10 million still using it—the pill appears to be relatively safe. There are undesirable side effects in some women. Among these are hypertension, acne, and abnormal bleeding. It also causes clotting of the blood in some women—but so does pregnancy. Such blood clots can clog a blood vessel and cause death by stroke or coronary heart attack. The death rate associated with the use of the pill is about 3 in 100 000. This is only one-tenth that associated with childbirth—about 30 in 100 000. For the general population, the pill is prob-

Figure 27.15 Carl Djerassi, professor of chemistry at Stanford University and president of Zoecon Corporation, Palo Alto, California.



19-Norprogesterone

Ethisterone

Mestranol

Norlutin

Figure 27.16 Some synthetic steroids.

ably as safe as aspirin. Women who have blood with an abnormal tendency to clot should not take the pill, nor should those who experience any serious side effects.

Recently, a "minipill" containing only a small amount of progestin and no estrogen has been marketed. It supposedly avoids many of the problems associated with the combination pill. Most of the undesirable side effects are thought to be caused by the estrogen.

Barring unforeseen developments, some form of chemical contraceptive seems to be with us to stay. The pill has already brought revolutionary social changes. The impact of science on society is perhaps nowhere more evident.

27.12 DES and the Morning After

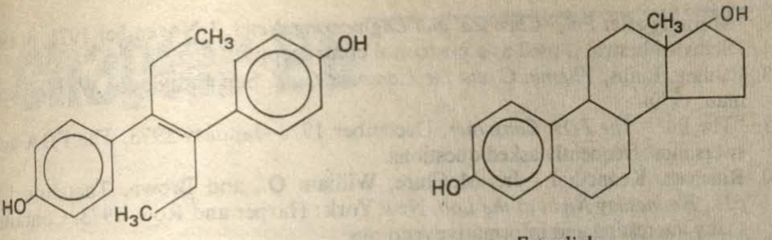
In 1973 the U.S. Food and Drug Administration approved the use of diethylstilbestrol (DES) to induce abortion. The action was surprising to some because DES had been banned earlier in 1973 as an additive in animal feeds. Cattle fed DES-treated feeds achieved marketable weights much more rapidly. The DES ban had a major impact on the cattle industry and was not undertaken lightly. The ban came only after a relation between DES and cancer was established. DES had been administered to women with a history of miscarriages in an attempt to *prevent* spontaneous abortion. No adverse effects were noted in these women. However, after 15 years, an abnormally high incidence of vaginal cancer was found among their daughters. This delayed effect points up one of the problems involved in evaluating a chemical for possible harmful effects.

As for banning the use of DES in animal feeds, the FDA had no choice. The Delaney clause of the Food and Drug Act of 1958 states clearly that any agent that causes cancer cannot be used in food. Despite efforts to prevent it, DES residues continued to appear in meat from animals that ate feeds containing this additive.

How could the FDA ban DES from animal feed and approve it as an abortifacient? The answer lies in the way the law is written and in the way the chemical is used. The Delaney clause *requires* the banning of any food additive that causes cancer in humans or laboratory animals. DES had been shown to cause vaginal cancers. Therefore, it had to be banned as a food additive. There is no such requirement for drugs; DES could be approved for use in inducing abortions. It was also pointed out that, if the drug was effective, there would be no offspring to have cancer.

DES is not a steroid. Examination of the shape of the molecule shows some similarity to that of estradiol (**figure 27.17**). Thus, DES is a synthetic female hormone. It was not significantly effective in maintaining pregnancy. Its use for that purpose (fortunately) was largely abandoned long before it was shown to cause cancer in the daughters of the women who took it. In order to induce abortion, one must take large doses. Unpleasant side effects are frequently noted.

Control of human reproduction is an area subject to great controversy—social, religious, political, and legal. Much more research is needed for our understanding of the biochemistry and physiology of human reproduction to be increased. One of the reasons that an effective male contraceptive has



DES *Estradiol*

Figure 27.17 The structures of DES and estradiol show slight similarities.

not been developed is that we know less about the male than the female reproductive system. Such research is certain to result in increased capabilities in drug design. Science will provide knowledge and materials. Ultimately, however, people must choose.

Problems

1. Define and give an example of each of the following.
   a. vitamin
   b. hormone
   c. provitamin
   d. androgen
   e. estrogen
2. In what ways do vitamins resemble hormones? In what ways do they differ?
3. For each of the vitamins discussed in this chapter indicate whether it is classed as water soluble or fat soluble, list a good food source of it, and list the disease or symptom caused by its deficiency.
4. How are vitamins related to coenzymes?
5. Does synthetic vitamin C differ from natural vitamin C?
6. If boiled vegetables are served as part of a meal, would the water-soluble or fat-soluble vitamins originally present be lost? Why?
7. Could a "one-a-month" vitamin pill satisfy all human requirements? Explain your answer.
8. Explain the role of vitamin A in the chemistry of vision.
9. Why is vitamin D called the "sunshine vitamin"?
10. What biochemicals are protected by vitamin E's antioxidant effect?
11. What is meant by the term *B complex*?
12. Describe the general sequence of events by which a nerve impulse is translated by the endocrine systems into a changed physiological state.
13. How does the birth control pill work?
14. What structural feature renders a synthetic steroid sex hormone effective orally?
15. Why can DES be used as a drug when it is banned as a food additive?

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chapter 28

Body Fluids

The processes of life occur for the most part in solution. The solvent for life processes is water, and the solutes are many—simple ions, small molecules, large molecules, and colloidal aggregates. These are found in a variety of body fluids, and each is essential in its own way to life.

A 70-kg (154-lb) person has about 5 ℓ of blood, including about 3 ℓ of plasma. That person has about 10 ℓ of interstitial fluid, the fluid which fills the space between cells. Fluid within the cells amounts to about 35 ℓ. Each day the individual excretes an average of 1.5 ℓ of fluid in urine, 0.2 ℓ of water in the feces, and 1 ℓ of water through the skin and lungs. All of these losses are balanced by water taken into or synthesized during metabolism within the body.

You are indeed a solution—or, rather, several solutions. But the solutions of which you are composed are not static; they constantly renew themselves. Because of this, their composition is quite dependent on the state of your health. Analysis of various body fluids represents one of the most powerful diagnostic techniques available to medical personnel.

28.1 Blood: An Introduction

Blood is the principal transport system of the human body. It carries (1) oxygen from the lungs to the tissues, (2) carbon dioxide from the tissues to the lungs, (3) nutrients from the intestines to the tissues, (4) metabolic wastes from the tissues to the excretory organs, (5) hormones from the endocrine glands to their target tissues, and (6) three major kinds of blood cells. In addition, blood helps maintain a fairly constant body temperature, an acid-base balance, an electrolyte balance, and a water balance. A rather remarkable substance, blood. And we've only mentioned a few highlights.

Blood makes up about 8% of the body's weight. Moderate amounts lost through bleeding or blood donation are readily replaced. **Table 28.1** contains a typical analysis of the blood of an average healthy adult.

Table 28.1
Analysis of the blood of a typical healthy adult

Component	*Amount*
Whole blood	
Blood volume	5 ℓ
Plasma volume	3 ℓ
Formed-cell volume (red cells, white cells, and platelets)	2 ℓ
Red cells	4 000 000/mm^3
White cells	7 000/mm^3
Platelets	300 000/mm^3
pH	7.4
Density	1.06 g/cm^3
Plasma	
Density	1.03 g/cm^3
Sodium ions (Na^+)	143 meq/ℓ
Potassium ions (K^+)	5 meq/ℓ
Calcium ions (Ca^{2+})	5 meq/ℓ
Magnesium ions (Mg^{2+})	2.5 meq/ℓ
Chloride ions (Cl^-)	103 meq/ℓ
Bicarbonate ions (HCO_3^-)	27 meq/ℓ
Hydrogen phosphate ions (HPO_4^{2-})	3 meq/ℓ
Sulfate ions (SO_4^{2-})	1 meq/ℓ
Organic acids	2 meq/ℓ
Proteins (albumin, globulin)	20 meq/ℓ

The formed
ts of blood.

Blood is a suspension of about 40% *formed elements* (red blood cells, white blood cells, and platelets) and about 60% fluid, called *plasma*. Normally, there are about 4 000 000 red blood cells, or *erythrocytes*, in each cubic millimetre of blood. If the number of red blood cells per cubic millimetre of blood is a good deal higher, a condition known as *polycythemia* exists. If the number is appreciably lower, a condition called *anemia* exists. Red blood cells are small and have no nucleus. They carry the respiratory protein hemoglobin. White blood cells, or *leukocytes*, are larger than the red blood cells (**figure 28.1**). They contain nuclei and exist in a variety of forms. Leukocytes attack infectious bacteria. Normally there are about 7000 white cells in each cubic millimetre of blood. The number rises sharply during some acute infections. An increase in white cell count characterizes the condition known as leukemia. In some cases of this disease, the leukocyte count may reach 500 000 per cubic millimetre of blood.

The third type of formed element is the *platelet*, or *thrombocyte*. These are even smaller than the red cells (**figure 28.1**). Like the red cells, they have no nucleus. There are usually about 300 000 platelets per cubic millimetre of blood. They are involved in the clotting of blood.

The fluid portion of the blood in which the formed elements are suspended is called *plasma*. Unless the blood is chemically treated, it is not possible to separate the plasma from the formed elements by filtration or any other technique. This is because freshly drawn blood tends to form clots on standing.

Clotting is not simply the precipitation of the formed elements, but a series of complicated chemical reactions (chapter 26). The fluid remaining after clotting occurs is called *serum* (not plasma). If one wishes to store blood plasma, an anticoagulant must be added to the freshly drawn blood to prevent clotting.

$$\text{Fresh blood } (+\text{ anticoagulant}) \longrightarrow \text{formed elements} + \text{plasma}$$

$$\text{Fresh blood} \longrightarrow \text{fibrinogen (clot)} + \text{formed elements} + \text{serum}$$

Plasma or serum can be separated from the solid materials by a centrifuge.

28.2 Electrolytes in Plasma and Erythrocytes

Plasma is about 90% water. Even red blood cells are about 65% water. A variety of ions are found in solution in both plasma and blood cells. These electrolytes play important roles in several life processes.

The concentration of electrolytes is often expressed as milliequivalents per litre (meq/ℓ) of fluid. Equivalent weights were discussed in chapter 11 for acids and bases. The milliequivalent weight of an ion is its atomic weight, expressed in milligrams, divided by the charge on the ion.

Example 28.1 What is the milliequivalent weight of Na^+?

The atomic weight of sodium is 23. The charge on the ion is 1 (the sign of the charge is ignored in these calculations).

$$\frac{23\text{ mg}}{1} = 23\text{ mg}$$

Example 28.2 What is the milliequivalent weight of Ca^{2+}?

The atomic weight of calcium is 40.

$$\frac{40\text{ mg}}{2} = 20\text{ mg}$$

Example 28.3 What is the milliequivalent weight of SO_4^{2-}?

The formula weight of the sulfate ion is 96.

$$\frac{96\text{ mg}}{2} = 48\text{ mg}$$

The number of milliequivalents in a certain amount of a substance is given by that amount (in milligrams) divided by the milliequivalent weight (i.e., the number of milligrams in a milliequivalent).

Example 28.4 How many milliequivalents are there in 30 mg of Ca^{2+}?

The milliequivalent weight of Ca^{2+} is 20 mg (example 28.2).

$$\frac{30\text{ mg}}{20\text{ mg/meq}} = 1.5\text{ meq}$$

Example 28.5 What is the concentration of Ca^{2+} in milliequivalents per litre if there are 12 mg of Ca^{2+} per 100 ml of serum?

First convert millilitres to litres.

$$\frac{12\ \text{mg}}{100\ \text{ml}} \times \frac{1000\ \text{ml}}{1\ \ell} = 120\ \text{mg}/\ell$$

The milliequivalent weight of Ca^{2+} is 20 mg. Therefore,

$$\frac{120\ \text{mg}/\ell}{20\ \text{mg/meq}} = 6.0\ \text{meq}/\ell$$

Typical electrolyte concentrations (in milliequivalents per litre) are given in **table 28.1.** Sometimes concentrations are expressed in milligram percents (milligrams per 100 ml) of plasma. To convert milligram percents to milliequivalents per litre, multiply the number of milligrams by 10 and then divide the result by the milliequivalent weight of the ion (example 28.5).

Sodium ions are found mainly in the plasma, and potassium ions are found chiefly in the erythrocytes. These positive ions do not migrate readily across cell membranes. Calcium and magnesium ions are the main dipositive ions in blood. They are usually determined in serum, because many anticoagulants added to preserve plasma tie up these ions. (Calcium ions are necessary for blood clotting; if they are removed, the blood will not clot.) Calcium ions are not found in erythrocytes, but magnesium ions are. The metabolism of calcium and the metabolism of phosphorus are closely related, and levels of the two usually vary in a reciprocal manner. Magnesium levels, on the other hand, are found sometimes to parallel the variations in calcium levels and at other times to parallel the variations of phosphorus levels.

The principal negative ions present in the blood, in addition to inorganic phosphorus (as HPO_4^{2-}), are chloride, bicarbonate, and sulfate. Bicarbonate and hydrogen phosphate are involved in the acid-base balance of the blood. These anions will be discussed in that regard in section 28.5.

Table 28.2 lists some conditions which influence plasma or serum levels of certain electrolytes.

28.3 Proteins in the Plasma

Proteins make up about 6.5% of the plasma. More than 20 different ones are present in plasma, the most important ones being *albumin*, the *globulins*, *fibrinogen*, and *prothrombin*. Fibrinogen and prothrombin are involved in the mechanism of blood clotting (chapter 26). The globulins and their role in the body's immune response will be discussed in section 28.4. All the proteins, but particularly albumin, are important in regulating the osmotic pressure of blood. To appreciate the significance of this function, it will be necessary for us to consider first a few facts about the movement of blood and its constituents.

How does material get from the blood to the cells? Diffusion of water, electrolytes, glucose, amino acids, and other materials occurs at a rapid rate through pores in the capillary walls. It occurs in both directions—from the blood into the interstitial fluid outside the capillary and from the interstitial fluid back into the blood. Diffusion through capillary walls occurs at a fan-

Table 28.2
Pathological conditions affecting electrolyte levels

	Diseases or Conditions Associated with Changes in Concentration	
Electrolyte	*Elevated Levels*	*Depressed Levels*
Sodium (Na^+)	Overactive adrenal glands	Severe kidney inflammation, Addison's disease (underactive adrenal cortex), pregnancy
Potassium (K^+)	Acute bronchial asthma, Addison's disease, uncontrolled diabetes, uremia	Hyperinsulinism (overproduction of insulin)
Calcium (Ca^{2+})	Overactive parathyroid	Underactive parathyroid, variety of kidney ailments, vitamin D deficiency
Magnesium (Mg^{2+})	Uremia, dehydration, Addison's disease, diabetic acidosis	Acute pancreatitis, chronic alcoholism
Chloride (Cl^-)	Kidney inflammation, heart disease	Burns, fever, pheumonia, vomiting, Addison's disease, diabetes
Hydrogen phosphate (HPO_4^{2-})	Uremia, nephritis, underactive parathyroid, overdose of vitamin D	Rickets, overactive parathyroid

tastic rate, estimated at equivalent to 1500 ℓ of water per minute for someone weighing 70 kg. Ultimately material makes its way from the interstitial space through cell walls and into (or out of) the cells themselves.

The blood doesn't just sit in the capillaries while the diffusion takes place. It circulates, that is, continues to move through the vascular system. What keeps the blood moving is the heart, a pump which pushes the blood around the system. The pressure imparted to the blood by this pumping action falls off as the blood travels from the heart through the arteries, the capillaries, and the veins and finally back to the heart, where it gets a fresh push. Blood moves from the high-pressure arterial end of the capillaries to the low-pressure venous end. As it circulates through the capillaries, the diffusion process described above occurs. The pressure which keeps the blood moving around the system also has a tendency to push the blood out of the porous capillaries into the interstitial space. In the absence of any countereffect, the rapid diffusion of material back and forth between blood and interstitial fluid would be accompanied by a slow but steady net loss of fluid from the blood to the interstitial space. Blood volume would drop and tissue would swell with the extra fluid. There is a countereffect, though—osmotic pressure.

Because both blood and interstitial fluid have all sorts of things dissolved in them, both fluids have characteristic osmotic pressures. Blood plasma has a higher one than interstitial fluid. Plasma contains proteins, molecules of colloidal size which cannot pass easily through the capillary pores into the interstitial compartment. Thus, whereas [illegible] plasma and interstitial fluid contain roughly equal concentrations of total electrolytes, the concentration of proteins (chiefly albumin) is higher in plasma than in interstitial fluid.

The proteins make a relatively small contribution to the osmotic pressure of plasma compared to the effect of the electrolytes. However, it is this smaller contribution which tips the scales in favor of the plasma.

Remember that the higher the osmotic pressure of a system the greater tendency it has to accumulate water (chapter 9). This means that in the capillaries there is a competition between two pressures—the *hydrostatic pressure* (the pressure which the heart's pumping action gives the blood) and the *colloid osmotic pressure* (the osmotic pressure due to the colloidal proteins in the blood, sometimes called *oncotic* pressure). The hydrostatic pressure pushes fluid out of the capillaries; the colloid osmotic pressure pulls liquid into the capillaries. Who wins? They both do.

At the arterial end of the capillaries the hydrostatic pressure (32 mm Hg) exceeds the colloid osmotic pressure (about 25 mm Hg), and there is a net loss of liquid to the interstitial space. At the venous end, the hydrostatic pressure is lower (15 mm Hg), but the colloid osmotic pressure is essentially unchanged (still about 25 mm Hg). At the venous end, then, the colloid osmotic pressure wins, and the net flow of fluid is into the capillary (**figure 28.2**). If we are in good health, everything balances rather nicely. To be sure, nutrients have diffused from blood to interstitial fluid and wastes have diffused from interstitial fluid to blood, but the volume of fluid in the two systems has remained constant.

If the concentration of plasma protein drops, the lowering of osmotic pressure results in a net flow of fluid to the interstitial space. The tissues become waterlogged and swollen, a condition known as *edema*. A lowering of the plasma protein level (and consequent edema) may be caused by liver disease, malnutrition, or nephrosis. Liver disease affects the protein level because albumin is made in the liver. In malnutrition, albumin production also drops off. Nephrosis is a condition in which albumin is lost into the urine (section 28.8).

The medical condition called *shock* also results from a loss of fluid from the vascular system. Capillary permeability increases and albumin is lost to

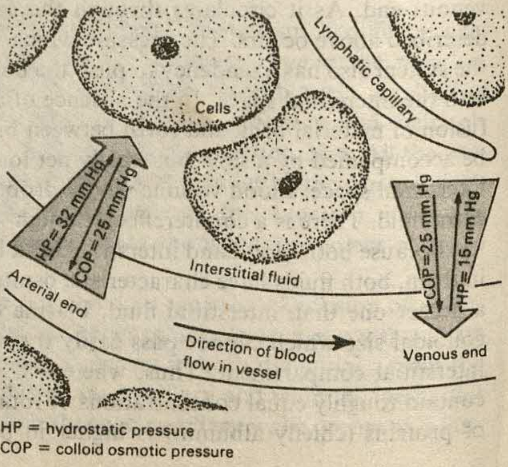


Figure 28.2 Net flow of fluids between capillary and interstitial fluid.

HP = hydrostatic pressure
COP = colloid osmotic pressure

the interstitial fluid. The resulting outflow of fluid from the vascular system reduces blood volume enough to cause a dramatic decrease in blood pressure. There is a consequent decrease in oxygen-transporting capability with potentially fatal results. When someone goes into shock following a traumatic injury, it means that the delicately balanced transport system in the body has gone awry and could fail completely. Shock is a physiological, not a psychological, state. Treatment of the condition involves bringing the blood volume back up to normal levels.

28.4 Gamma Globulins: The Good and Bad of Immunity

Some of the plasma proteins, the *gamma globulins*, are associated with a sophisticated defense mechanism in the body termed the *immune response*. When the body is invaded by foreign macromolecules (such as proteins), it responds by synthesizing its own specialized proteins called *antibodies* (also called immunoglobulins). Since the foreign substance triggers the synthesis of antibodies, the invader is called an *antigen* (it causes antibody generation). Each distinctive antigen causes a unique set of antibodies to be produced. The antibodies are designed to lock onto the particular antigen. They bind to it and, to oversimplify a bit, incapacitate it. In some instances the incapacitation involves the formation of a precipitate, with the antigen being tied up as part of an antibody-antigen clot.

When the body is invaded by pathogenic antigens (disease-causing bacteria or viruses, for example), its ability to produce specific antibodies represents an effective defense mechanism. It is even possible to prime this mechanism. A *vaccine* containing a weakened form of the antigen (dead bacteria, for example) will cause an individual to build up a certain level of antibodies for this particular antigen. If the same individual is then subjected to attack by a more virulent form of the antigen, the body responds much more rapidly and effectively to its presence. Having practiced on the dead "bug," the system can easily handle the live one; it has gained an immunity to that particular organism.

Figure 28.3 Smallpox, which once killed and disfigured millions, may have been completely eradicated by the time you read this. (Courtesy of the U.S. Agency for International Development, Washington, D.C.)

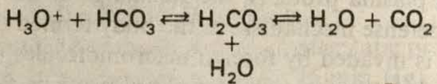
Unfortunately, the body can't tell "good" antigens from "bad" antigens. We want it to respond to a viral infection, but we wish it wouldn't attack purposely transplanted tissue. Nonetheless, the host body will respond to a donor skin graft, a kidney transplant, or a heart transplant as it does to a virus, by generating antibodies to attack it. When the body responds to foreign tissues in this way, the process is called *rejection*. This is a major problem associated with organ transplants. There are drugs which suppress the immune response, but when these are used on a transplant recipient to protect the transplanted organ, the patient also becomes more susceptible to infection. If you turn off the immune response, you turn off both the good and bad aspects of it.

Research in immunology is directed toward developing selective immune responses. If some cancers are caused by viruses, can we develop effective anticancer vaccines? Can we keep a body from rejecting a transplanted heart while maintaining its immune response to pathogenic microorganisms? Immunochemists and immunologists are trying to answer such questions.

28.5 A Balancing Act: Acids and Bases in the Blood

In chapter 11, we examined buffer systems in general and blood buffers in particular. You will recall that the pH of the blood must be maintained within a very narrow range around 7.4. If it falls below 7.35, *acidosis* sets in. If it rises above 7.45, a condition called *alkalosis* exists. The life-sustaining range of blood pH covers only 1 pH unit—from about 6.8 to about 7.8.

The primary blood buffer is the bicarbonate/carbonic acid system (HCO_3^-/H_2CO_3). The buffering power of this system is enhanced by the interconversion of carbonic acid and carbon dioxide, so that the entire system can be represented as



$$H_3O^+ + HCO_3 \rightleftharpoons \underset{\substack{+\\ H_2O}}{H_2CO_3} \rightleftharpoons H_2O + CO_2$$

Addition of acid shifts the equilibrium to the right, tying up hydronium ions. Added base will cause a shift to the left, releasing hydronium ions.

In certain situations, the buffers can be overwhelmed or may fail to function properly, and acidosis or alkalosis can result. If a person hyperventilates (breathes in and out very rapidly), too much carbon dioxide can be exhausted. This ultimately results in a shift in the equilibrium to the right. As hydronium ions are tied up, the pH increases and respiratory alkalosis occurs. If an individual is not ventilating adequately (because of some lung obstruction or disease, for example), carbon dioxide builds up in the blood, the equilibrium shifts to the left, more hydronium ions are released, the pH falls, and respiratory acidosis occurs. Metabolic disorders are more likely to produce acidosis than alkalosis because metabolism produces a variety of acids, including lactic, pyruvic, and phosphoric acids, as well as carbonic acid. We will discuss acidosis further in chapter 31.

Other plasma buffers are the monohydrogen phosphate/dihydrogen phosphate system and the plasma proteins. The latter, which have both acidic and basic groups on the side chains of certain amino acid residues, can give up protons if the blood starts to get alkaline or accept protons if the blood starts to get acidic.

The bicarbonate/carbonic acid buffer system also operates within the red blood cells. Here it is coordinated with two important hemoglobin buffers also found in the erythrocytes. We will look more closely at hemoglobin and its role in oxygen transport shortly. For now let's consider the interplay of the hemoglobin and bicarbonate/carbonic acid buffers. One of the hemoglobin buffers can be represented as HHb for the acidic form and Hb^- for the basic form.

Carbon dioxide produced by cell respiration diffuses into red blood cells. In the red blood cells, the carbon dioxide is rapidly converted to carbonic acid.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3$$

The carbonic acid reacts with the basic form of hemoglobin, yielding the acidic form of hemoglobin and bicarbonate ion.

$$H_2CO_3 + Hb^- \rightleftharpoons HCO_3^- + HHb$$

Bicarbonate builds up in the cell. It has a tendency to diffuse out, but electrical neutrality must be preserved. Positive potassium ions in the erythrocytes won't cross the cell membrane readily, so neutrality is maintained by another negative ion, chloride, which diffuses in as bicarbonate moves out. This phenomenon is called the *chloride shift*. At equilibrium, about 60% of the bicarbonate ion is in the plasma, and 40% is in the erythrocytes.

When the blood reaches the lungs, hemoglobin picks up fresh oxygen form oxyhemoglobin, which we'll write for now as $HHbO_2$. This molecule is the acidic form of the second hemoglobin buffer. The basic form we'll write as HbO_2^-. In the capillaries of the lungs, the acidic oxyhemoglobin reacts with the bicarbonate ion accumulated by the erythrocytes.

$$HHbO_2 + HCO_3^- \dashrightarrow HbO_2^- + H_2CO_3$$

The carbonic acid thus produced is rapidly converted to carbon dioxide,

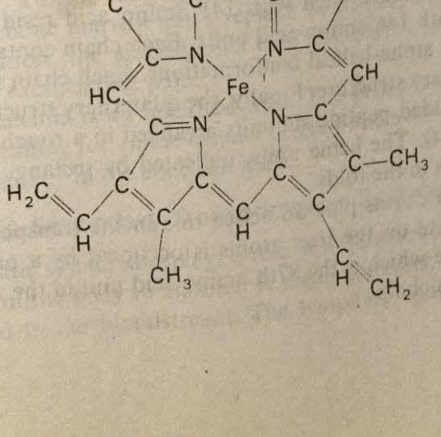
$$H_2CO_3 \longrightarrow H_2O + CO_2$$

and the carbon dioxide is exhausted through the lungs to the atmosphere.

Through these acid-base reactions, hemoglobin plays a role in the transport of carbon dioxide from cells to the lungs. Its role as an oxygen carrier is discussed in the next section.

28.6 Hemoglobin: Or How to Carry an Oxygen Molecule (or Two or Three or Four)

One of the main functions of blood is the transport of oxygen. The oxygen-carrying component is a conjugated protein called hemoglobin. The hemoglobin molecule has a protein portion and a nonprotein portion, or prosthetic group. The prosthetic group is heme.



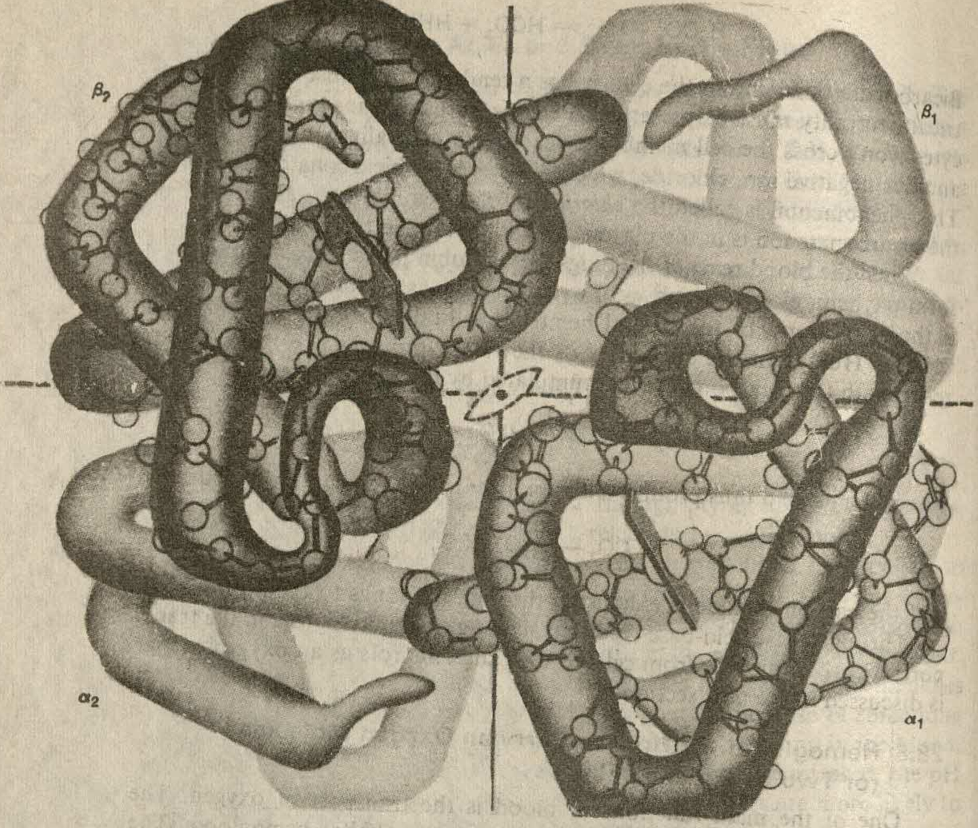
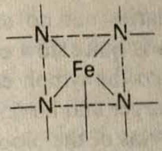


Figure 28.4 The quaternary structure of hemoglobin. The four protein units are designated α_1, α_2, β_1, and β_2. (Reprinted with permission from Gutsche, C. David, and Pasto, Daniel J., *Fundamentals of Organic Chemistry,* Englewood Cliffs, N.J.: Prentice-Hall, 1975. Copyright © 1975 by Prentice-Hall, Inc.)

A hemoglobin molecule contains four heme units, each with a central iron atom. This iron atom in each heme unit is attached to the nitrogen atoms of four pyrrole rings (chapter 19). It is in the +2 oxidation state and is capable of forming two additional bonds.

The protein portion of the hemoglobin molecule has four polypeptide chains, which are not covalently bonded to one another. There are two identical alpha chains, each with 141 amino acid residues, and two beta chains, each with 146 amino acid units. Each chain contains sections which are coiled into alpha-helical conformations. Each chain is then folded into a globular tertiary structure. Finally, the quaternary structure of this protein has the four folded peptide subunits arranged in a roughly tetrahedral pattern (**figure 28.4**). The heme units, indicated by rectangular shapes, are located in cavities in the folds.

The protein chains play an active role in the transport of oxygen. The fifth bonding site on the iron atoms is occupied by a nitrogen atom of a histidine residue which is the 87th amino acid unit in the alpha chain or the 92nd in the beta chain.



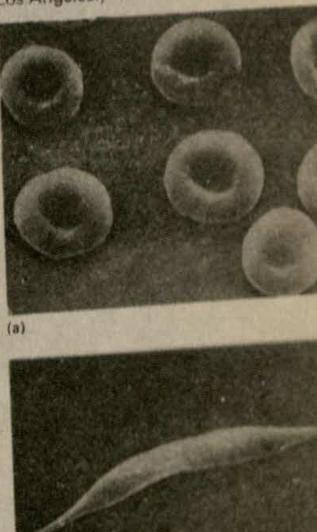
Each hemoglobin molecule is capable of transporting four molecules of oxygen; each oxygen molecule occupies the sixth bonding site of an iron in one of the heme units. Binding of one oxygen molecule facilitates the attachment of another, because oxygenation changes the conformation of the chain. This seems also to induce changes in a neighboring heme-peptide unit, giving it a greater affinity for oxygen. Conversely, release of oxygen from one site facilitates release from a neighboring site. These factors enable hemoglobin to load and unload oxygen quite rapidly.

Normally, there are about 15 g of hemoglobin per 100 ml of blood. This amount of hemoglobin can combine with about 20 ml of gaseous oxygen (at STP). Without the hemoglobin, only 0.3 ml of gaseous oxygen could physically dissolve in 100 ml of plasma.

Red blood cells are manufactured in the bone marrow. The life span of a red blood cell is about 120 days. After that amount of time, the hemoglobin in the cell breaks down. The protein portion (globin) is metabolized like other proteins. The heme portion breaks down into bilirubin, a yellow-brown pigment, and other products. Bilirubin is the chief bile pigment. It is further changed to other colored compounds which are excreted. These give urine and feces their characteristic colors. The sometimes spectacular color changes observed in a bruise have a related cause. A bruise consists of blood released and trapped beneath the skin. As the blood is gradually broken down, a series of colored products is formed.

There are a variety of *abnormal hemoglobins*, each responsible for a particular disease. Perhaps the most notorious of the abnormal hemoglobins is that responsible for sickle cell anemia. This hemoglobin, called hemoglobin S (HbS) differs from ordinary hemoglobin in only one amino acid: at the sixth position of the beta chains, hemoglobin S has valine rather than glutamic acid. This seemingly minor variation not only changes the conformation of oxyhemoglobin but causes the red blood cells themselves to change from a round to a sickle shape (**figure 28.5**). These sickled cells are rapidly destroyed. The bone marrow can't replace them fast enough, and anemia results. In addition, the sickled cells clog capillaries, particularly in the spleen, causing excruciating pain.

Figure 28.5 (a) Normal red blood cells. (b) Sickled cells. (Courtesy of Richard F. Baker, University of Southern California Medical School, Los Angeles.)



Sickle cell anemia is an inherited trait. The genetic code has one error in its message, calling for valine instead of glutamic acid. What a difference one minor "mistake" in the code can make.

28.7 Lymph: A Secondary Transportation System

The lymphatic system also plays a role in the transportation of materials from one part of the body to another. It seems to return components of the interstitial fluid to the bloodstream. The lymphatic system (**figure 28.6**) is

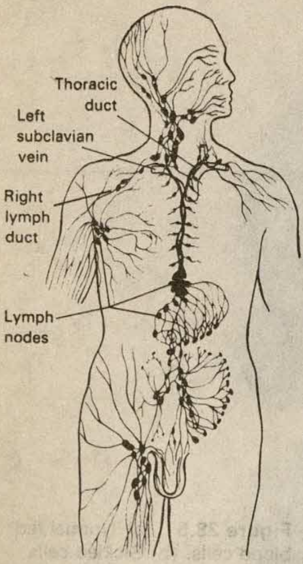


Figure 28.6 The lymphatic system.

composed of veins and capillaries but no arteries. Lymph capillaries are closed at one end. Lymph flow is quite slow compared to blood circulation. Interstitial fluid is absorbed into the lymph capillaries, in which it is called *lymph.* This lymph flows into larger and larger lymph veins. Eventually, two large lymph veins empty into veins of the blood circulatory system.

Lymph serves other functions. Fat absorbed in the intestine is picked up by lymph capillaries rather than blood capillaries. Lymph *nodes* serve as filters and as factories for the production of some forms of white blood cells. The white blood cells located there remove dead cells, bacteria, and other foreign elements from the lymph. It is in the nodes that antibodies are synthesized. These nodes are lumpy enlargements in the lymph veins. Sometimes the nodes are so effective at filtering out bacteria from an infected area that they become swollen. Someone suffering from a sore throat may also exhibit swollen and tender lymph nodes in the neck area.

The role of lymph, though secondary to that of blood, is nonetheless an important one.

28.8 Urine: Formation and Composition

The kidneys operate to remove metabolic waste products from the blood. The functional units of the kidneys are called *nephrons* (**figure 28.7**). Each nephron has a bulbous *Bowman's capsule,* which tails into a long, highly convoluted urinary tubule. The capsule surrounds a network of arterial capillaries called the *glomerulus.* These capillaries rejoin to form a small artery (arteriole) and then divide into another network of capillaries that surrounds

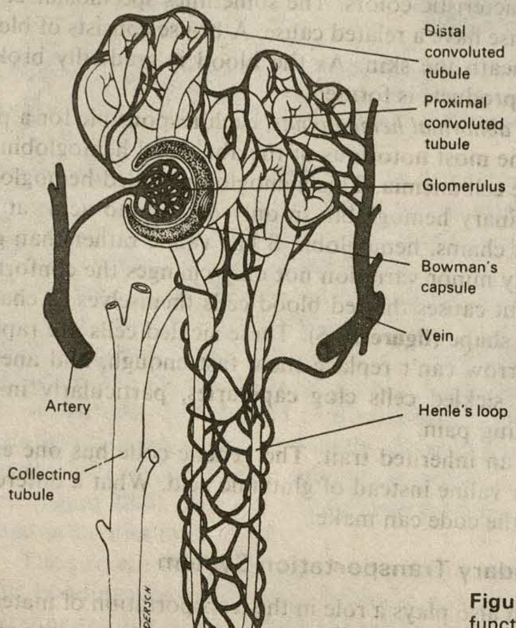


Figure 28.7 Nephrons are the functional units of kidneys, where metabolic wastes are removed from the blood.

the tubule of the nephron. Finally these capillaries join again and form a small vein. Blood flows from the artery into the glomerulus (capillaries), then through the arteriole and the second capillary network surrounding the tubule, and finally out the vein (**figure 28.8**).

Most of the constituents of the blood, except the formed bodies and large protein molecules, are filtered out through the capillary walls of the glomerulus. The glomerulus seems to act as a simple filter, with particle size being the main factor that decides what goes and what stays. The fluid that enters Bowman's capsule and eventually collects in the tubule contains many valuable components as well as wastes. Consider water alone. About 170 ℓ per day are filtered into the tubules. Most of this water—and valuable constituents such as glucose, amino acids, and salt—are reabsorbed by the blood through the walls of the tubules. Waste products, such as urea, uric acid, and excess salts, are passed on into collecting tubules and eventually excreted as *urine*. Knowing that healthy adults pass 1.1 to 1.5 ℓ of urine each day, you can calculate that over 99% of the water that is filtered through the glomerulus is reabsorbed through the tubules. We'd have quite a drinking problem if all that water weren't conserved.

The amount and composition of the urine is quite variable. Its volume depends on liquid intake, amount of perspiration, presence of fever or diarrhea, and other factors. The composition varies with diet and state of health. Most substances have a kidney threshold level. If the concentration of a substance in the blood exceeds this threshold value, the excess is not reabsorbed through the tubule but appears in the urine. The threshold level for glucose (blood sugar), for example, is quite high. Normally, nearly all glucose is reabsorbed. If the glucose level in the blood is too high, however, glucose shows up in the urine (as happens in cases of uncontrolled diabetes).

Some components of urine have a relatively low solubility. When some

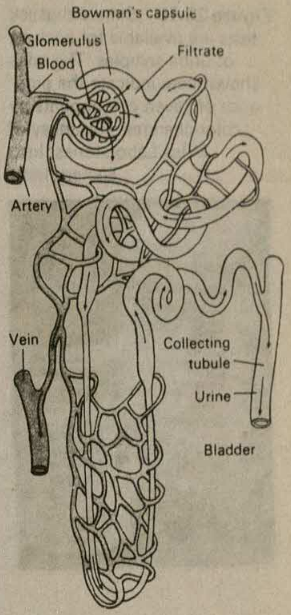


Figure 28.8 This view of a nephron indicates the path of fluids through the unit.

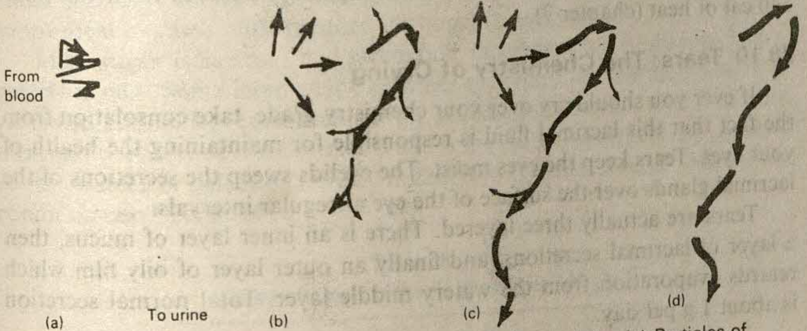


Figure 28.9 The fates of various substances in the kidney tubule. (a) Particles of colloidal size (proteins) or larger (blood cells) never filter into Bowman's capsule and, therefore, do not ordinarily appear in urine. (b) Substances with a high threshold (glucose, etc.) filter into the tubules but are then reabsorbed by the blood. They do not ordinarily appear in urine. (c) Substances with intermediate thresholds (inorganic ions such as Na^+ or Cl^-) filter into Bowman's capsule and are then partially reabsorbed by the blood. Dietary levels determine how much finally remains in urine. (d) Substances with low thresholds filter into the tubule and remain there. Urine is rich in urea.

Figure 28.10 Simple dipstick tests are available for analysis of urine samples. The ones shown here indicate the presence of seven components by color changes. (Courtesy of Miles Laboratories, Inc., Elkhart, Ind.)

condition (such as an increase in concentration or a change in pH) leads to the precipitation of these materials in the kidney, a stone is formed. Kidney stones (or *renal calculi*) usually consist of calcium phosphate [$Ca_3(PO_4)_2$], magnesium ammonium phosphate ($MgNH_4PO_4$), calcium carbonate ($CaCO_3$), calcium oxalate (CaC_2O_4), or a mixture of these. Stone formation may accompany increased concentration of calcium ion caused by disease or increased ingestion of calcium ion. People who eat foods rich in oxalates (such as spinach) have a relatively high incidence of oxalate kidney stones. (What a great excuse for kids who don't want to eat their spinach!)

The kidney does far more than just get rid of wastes. It plays a vital role in maintaining the balance of water, electrolytes, acids and bases, and other components of the body fluid. When the kidneys malfunction, the body is in trouble. Analysis of the urine can often give a good indication of the health of the individual.

28.9 By the Sweat of Our Brow

The skin is also an organ of excretion. Through it we lose water, electrolytes, nitrogenous wastes, and lipids. Water is lost directly through the skin and through the respiratory tract at a rate of about 700 ml per day. This water loss is called *insensible perspiration*. Perspiration from the 2.5 million sweat glands is called *sensible perspiration*. It is activated by a rise in blood temperature.

Sweat is about 99% water. It contains sodium ions, chloride ions, calcium ions, and smaller amounts of other minerals. A person working in a hot environment might lose 12 ℓ of sweat per day, including 70 g of salt. Organic constituents of sweat include urea, lipids (body oils), creatinine, lactic acid,* and pyruvic acid. Drugs such as morphine, nicotine, and alcohol will also appear in sweat.

If the air around us is not too humid, the water in sweat evaporates. Perspiration carries off not only wastes but also heat. It helps us keep cool on hot days. Each gram of water that evaporates absorbs from the body 540 cal of heat (chapter 7).

28.10 Tears: The Chemistry of Crying

If ever you should cry over your chemistry grade, take consolation from the fact that this lacrimal fluid is responsible for maintaining the health of your eyes. Tears keep the eyes moist. The eyelids sweep the secretions of the lacrimal glands over the surface of the eye at regular intervals.

Tears are actually three layered. There is an inner layer of mucus, then a layer of lacrimal secretions, and finally an outer layer of oily film which retards evaporation from the watery middle layer. Total normal secretion is about 1 g per day.

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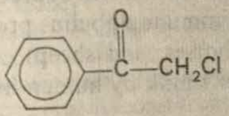
*It is interesting to note that female mosquitoes, seeking their meal of blood, find us by following a warm stream of air laden with carbon dioxide and lactic acid. We could foil them by not sweating and not breathing!

Chemically, tears have about the same composition as other body fluids. They have approximately the same salt content as blood plasma. Tears contain *lysozyme*, an enzyme that ruptures bacterial cell walls. This bactericidal action helps prevent eye infections.

Copious flows of tears may be caused by irritants, such as pepper, acid fumes, or a variety of chemical lachrymators. Tear gas, usually α-chloroacetophenone, is a specially designed eye irritant.



The flow of tears may also be triggered by emotional upsets. Such crying is undoubtedly controlled by hormones. And if you feel like crying, go right ahead. Most psychologists say it's good for you. Indeed, many people have long believed crying to be beneficial. Richard Crashaw, an English poet of the 17th century, called tears "the ease of woe."

28.11 The Chemistry of Mother's Milk

Newborn mammals are nourished by a secretion of the mammary glands of their mothers. Indeed, the presence of such glands in females characterizes the class Mammalia. The composition of milk varies from one species to another (**table 28.3**). Amounts of fat and protein tend to be greater in marine mammals and those that live in cold climates.

Colloidal proteins and emulsified fats give milk its characteristic milky appearance. *Casein* is the precipitated protein from cow's milk. Humans beyond infancy generally include some milk or milk products in their diet. This food is an excellent source of most nutrients. It includes all the essential amino acids. It also contains most vitamins and minerals. Cow's milk, though, is a poor source of iron, copper, and vitamin C. It is also short of vitamin D as it comes from the cow, but this vitamin is often added as a supplement to cow's milk intended for human consumption.

Milk sugar is lactose, a disaccharide incorporating a glucose and a galactose unit. Some infants lack enzymes necessary for the metabolism of galactose and suffer from a condition called *galactosemia*. Children with this condition may develop cataracts and some mental disorders. By removal of the sources of galactose (chiefly milk) from the diet of such infants, the condition can be controlled.

Table 28.3

Composition of milks (in grams per 100 g)

Mammal	*Fat*	*Protein*	*Lactose*
Cow	4.4	3.8	4.9
Human	3.8	1.6	7.0
Goat	4.1	3.7	4.2
Reindeer	22.5	10.3	2.5
Porpoise	49.0	11.0	1.3

Cow's milk is sometimes given to infant humans as a substitute for their mother's milk. Recent evidence indicates that this may not be a wise substitution. Human milk not only more closely matches the nutritional needs of human infants, but it may also add to the infant's immunological defenses against disease. Newborn infants are unable to make antibodies. They have *temporary passive immunity* because their blood contains antibodies made by the mother and passed across the placenta. Mother's milk produced within the first few days after childbirth is a rich source of gamma globulins. There is clear evidence that these immunoglobulins protect some newborn animals (ungulates such as cows, horses, and sheep). A similar utilization of the immunoglobulins in mother's milk by human infants has not yet been conclusively proven.

Problems

1. List five functions of the blood.
2. How are plasma and serum obtained from whole blood?
3. What blood electrolyte is required for clotting?
4. What is a *formed element* of the blood?
5. What is an erythrocyte? A leukocyte? A thrombocyte? What is the function of each?
6. What are four protein fractions in plasma?
7. Name four positively charged and four negatively charged ions in blood plasma.
8. a. The concentration of electrolytes in the spinal fluid of a patient was reported in milligram percent. Calculate the corresponding values in milliequivalents per litre.

   $Cl^- = 426$ mg %

   $Ca^{2+} = 2.5$ mg %

   $Na^+ = 322$ mg %

   b. The normal values for these ions in spinal fluid fall within the following ranges.

   Cl^-: 118–132 meq/*l*

   Ca^{2+}: 2.1–2.9 meq/*l*

   Na^+: 138–158 meq/*l*

   Does the analysis of this patient's spinal fluid (given in part a) reveal any abnormalities?
9. What is interstitial fluid? What is lymph?
10. Explain the role of diffusion, blood pressure (hydrostatic pressure), and oncotic pressure (colloid osmotic pressure) in transferring material from capillaries to interstitial fluid and vice versa.
11. What is edema? What causes it?
12. What is shock?
13. What are the three main buffers in blood?
14. Using equations, explain how the bicarbonate/carbonic acid buffer would combat acidosis. How would it combat alkalosis?
15. What condition results in respiratory acidosis? In respiratory alkalosis? In metabolic acidosis?
16. Explain the role of the hemoglobin buffers in carbon dioxide transport.
17. What is the chloride shift? Why does it occur?
18. What are antibodies? What are antigens?

19. Describe the immune response.
20. In what blood protein fraction are antibodies found? Where are antibodies formed?
21. What is a vaccine?
22. How are immunity and tissue rejection related?
23. Which of the body fluids functions to cool the body? By what mechanism does it work?
24. Give a general description of the hemoglobin molecule.
25. What is the source of bilirubin?
26. List three functions of the lymphatic system.
27. How is urine formed in the kidney?
28. List four factors that affect the volume of urine excreted.
29. List three organic components of urine.
30. What is the difference between sensible and insensible perspiration?
31. List three inorganic and three organic constituents of sweat.
32. What are the three layers of tears?
33. What is the function of lysozyme in tears?
34. Is cow's milk a "perfect" food? Does it contain a complete protein?
35. What advantage does human milk possess over cow's milk as a food for a human infant?

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chapter 29

Digestion

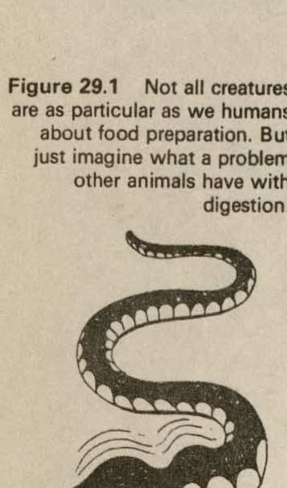

YOU HUMANS ALWAYS FUSS SO MUCH WITH YOUR FOOD. (BURP!) I BEG YOUR PARDON.

Figure 29.1 Not all creatures are as particular as we humans about food preparation. But just imagine what a problem other animals have with digestion.

There on the table are some carbohydrates, lipids, and proteins, small portions of vitamins and minerals, and a generous dollop of water. What we want to do is to get all of these nutrients from the table to our cells. So we cook our meat and potatoes, cut them into small pieces, and proceed to eat.

The cooking and cutting has not prepared the food adequately for absorption into our bodies, however. Our cells demand a much more highly refined form of the basic nutrients. The huge complex molecules that constitute proteins, carbohydrates, and, to some extent, lipids must be broken down to simpler, more soluble substances. This process, called *digestion,* must occur before food can really be taken *into* the body. It is carried out in the *digestive tract,* a tunnel that runs *through* the body. Food in the digestive tract is in the tunnel, not *in* the body. The alternative name for the digestive tract, *the alimentary canal,* perhaps conveys this image more clearly.

Food is sluiced through the canal by a flow of digestive juices and by physical pushes imparted by sections of the canal. Compounds that are changed during this journey into suitable forms are absorbed through the walls of the canal into the circulatory systems of the body. Those materials which can't be absorbed make their way through the entire length of the canal and out again. Without the process of digestion, very little of the food we eat would nourish us.

29.1 The Digestive Tract and the Nature of Digestion

The structures that make up the digestive tract are the mouth, pharynx (throat), esophagus, stomach, small intestine, large intestine, rectum, and anus. Other structures associated with the tract itself are the salivary glands, liver, gallbladder, and pancreas. **Figure 29.2** shows these structures somewhat schematically. Note that the first section of the small intestine, where it joins the stomach, is called the duodenum. Pancreatic juice and bile enter the digestive tract here.

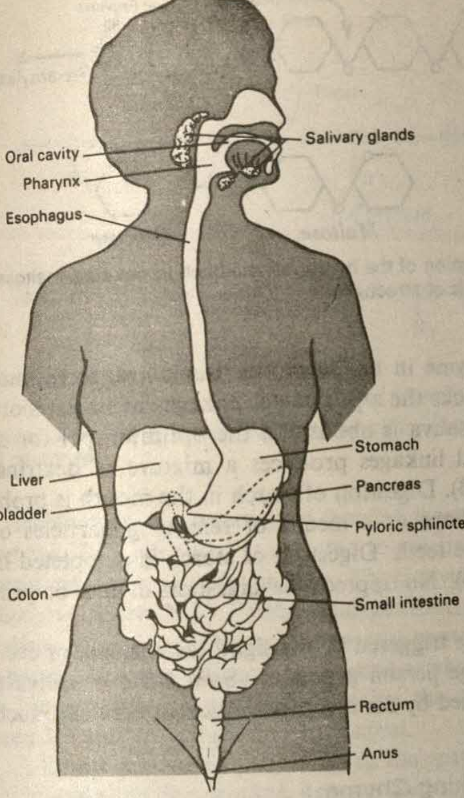


Figure 29.2 The human digestive system, showing the organs somewhat displaced for clearer viewing. The small intestine is much longer than indicated here.

Digestion is hydrolysis. Fats (esters) are hydrolyzed to glycerol and fatty acids. Proteins (polyamides) are hydrolyzed to amino acids. Polysaccharides and disaccharides (polyacetals) are hydrolyzed to monosaccharides. Nucleic acids (polynucleotides) are hydrolyzed to nucleotides and then to nucleosides and phosphoric acid.

Water for these hydrolysis reactions is present in saliva and the other *digestive juices*. Each step is catalyzed by specific enzymes. Each enzyme operates at or near its optimum pH and at body temperature (37 °C). Without the enzymes, no appreciable hydrolysis would occur.

29.2 The Way to Salivation: The Mouth

Enzymatic digestion starts in the mouth. Here the food encounters *saliva*, a digestive fluid secreted by the salivary glands. Saliva is over 99% water. It contains several inorganic ions and a variety of organic molecules typical of other body fluids. In the mouth, food is chewed, that is, torn or crushed to a finer consistency. Reduction of food to smaller particles facilitates digestion by providing greater surface area for enzymes to work on. Chewing also coats the food particles with *mucin*, a glycoprotein constituent of saliva. The mucin lubricates the food and makes it easier to swallow.

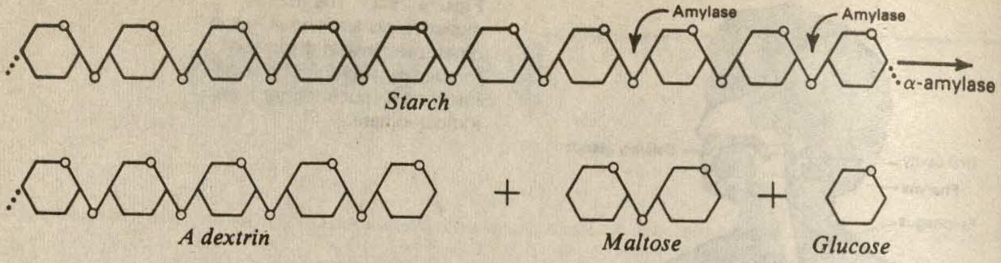


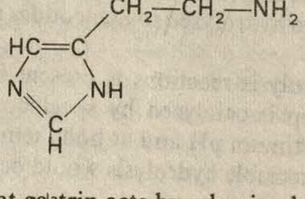
Figure 29.3 A schematic representation of the hydrolysis of starch to dextrins, maltose, and glucose. See chapter 22 for details of structure.

The principal digestive enzyme in the mouth is *α-amylase,* sometimes called ptyalin. This enzyme attacks the alpha acetal linkages in starch more or less at random. The pH of saliva is about 6.8, the optimum pH for α-amylase. Cleavage of the acetal linkages produces a mixture of dextrins, maltose, and glucose (**figure 29.3**). Digestion of starch in the mouth is probably not necessary, except perhaps as a means of removing particles of starchy food lodged between the teeth. Digestion of starch is completed in the small intestine (section 29.4). No appreciable digestion of fats or proteins occurs in the mouth.

The secretion of saliva can be triggered by the sight, taste, smell, or even the thought of food. An average person produces about 1.5 ℓ of saliva a day. Excessive flow may be caused by certain pathological conditions, such as mercury poisoning.

29.3 Gastric Digestion: Making Chyme

Gastric juice is a mixture of secretions of the stomach. The chief components are water (more than 99%), mucin, the usual inorganic ions, hydrochloric acid, and some enzymes. A protein hormone called *gastrin,* produced in the stomach, starts the flow of gastric juices. Flow can also be started by histamine.



Indeed, it may well be that gastrin acts by releasing histamine, which in turn stimulates the secretion of gastric juices.

Hydrochloric acid is secreted by certain glands in the lining of the stomach. The pH of freshly secreted gastric juice is about 1.0, but contents of the stomach may partially neutralize it, raising the pH to from 1.5 to 2.5. (The pain of a gastric ulcer is at least partially due to the irritation of the ulcerated tissue by the acidic gastric fluid.) Hydrochloric acid is involved in the denaturation of food protein; it opens up the folds to expose the chains to more efficient enzyme action. Hydrochloric acid is also involved in the activation of *pepsin,* a protein-splitting enzyme.

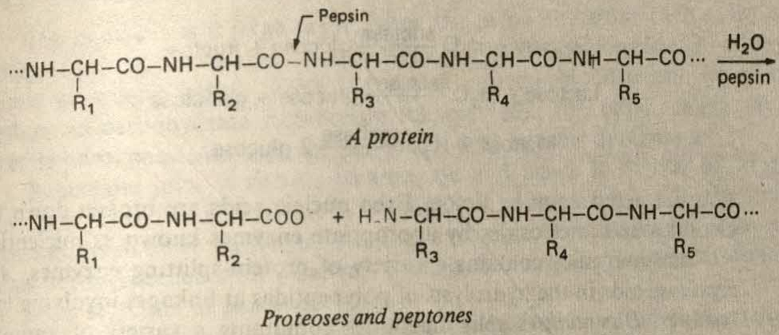


Figure 29.4 Pepsin breaks down proteins into soluble fragments called proteoses and peptones.

Pepsinogen is a proenzyme secreted from certain cells in the wall of the stomach. It is activated (converted to pepsin) by hydrochloric acid and by pepsin which is already present. The activation by pepsin is called autocatalysis (section 26.7). Pepsin catalyzes the hydrolysis of proteins into intermediate products called proteoses and peptones (**figure 29.4**). It acts only on peptide linkages adjacent to tyrosine or phenylalanine units. The optimum pH for pepsin is about 2, which makes the gastric fluid, with its pH of between 1.5 and 2.5, an ideal environment.

A lipase enzyme is also found in the gastric juice. It may be there only accidentally, having worked its way back up from the small intestine. At any rate, gastric lipase does very little in the way of digesting fats in the stomach, for its optimum pH is near 7, far from the pH of the stomach contents.

Another product of the stomach factory is a mucoprotein called *intrinsic factor*. This substance is essential to the absorption of vitamin B_{12}. *Pernicious anemia* is characterized by the failure of the stomach lining to produce intrinsic factor. Treatment of choice for pernicious anemia is injection of vitamin B_{12}.

Food stays in the stomach for from 2 to 5 hours. It is broken down by pepsin and by the mechanical churning of the stomach into a thin, watery liquid called *chyme*. This material then passes, in small portions, into the *duodenum*, the first 30 cm (12 in.) of the small intestine.

29.4 Intestinal Juice: Taking It All Apart

As far as digestion is concerned, the small intestine is where the action is. The process, barely started in the mouth and carried forward only slightly in the stomach, is completed in the small intestine. Much coiled, the small intestine is about 7 m (23 ft) long in adult humans. Most of the enzymes of the intestinal juice are secreted from the duodenum.

Intestinal juice is involved in hydrolysis of all classes of foodstuffs. Several protein-splitters complete the hydrolysis of proteins to amino acids. The disaccharides sucrose, lactose, and maltose are hydrolyzed to monosaccharides by enzymes secreted by the intestinal mucosa, as summarized by these word equations.

$$\text{Sucrose} + H_2O \xrightarrow{\text{sucrase}} \text{glucose} + \text{fructose}$$

$$\text{Lactose} + H_2O \xrightarrow{\text{lactase*}} \text{glucose} + \text{galactose}$$

$$\text{Maltose} + H_2O \xrightarrow{\text{maltase}} 2\ \text{glucose}$$

Fats are acted upon by lipase. Even nucleic acids are broken down to nucleotides and nucleosides by appropriate enzymes known as nucleotidases.

Intestinal juice contains a variety of protein-splitting enzymes. *Aminopeptidase* aids in the hydrolysis of polypeptides at linkages involving leucine residues. *Dipeptidases* split dipeptides containing a variety of amino acid units. Perhaps most interesting, though, is *enterokinase*. This enzyme converts the proenzyme *trypsinogen,* which comes from the pancreas, into *trypsin,* an active protein-splitting enzyme.

Many of the intestinal enzymes work right in the cells of the intestinal mucosa, not out in the hollow tube itself. Thus, final hydrolysis may be completed in the cells of the intestinal wall as the nutrients diffuse through.

Most of the absorption of digested foods takes place in the lower digestive tract, particularly in the small intestine. (Alcohol is an exception to this rule: it can be absorbed while still in the stomach. That means it gets into the bloodstream faster than most foods.) The inner walls of the intestines are lined with millions of microscopic projections called *villi* (**figure 29.5**). The presence of the villi greatly increases the effective surface area of the intestine, providing much more contact between the digested foodstuffs and the absorbing surface of the intestinal wall. **Figure 29.6** shows a detailed view of one of the villi. The structure is richly supplied with blood and lymph vessels. Nutrients pass through the walls of the villi and are absorbed by blood (or lymph, in the case of fats). The transport across cell walls involves energy, which requires cell activity. Thus, the absorption of nutrients from the intestines is not simply a matter of passive diffusion but of active transport in which cells participate in moving the material through.

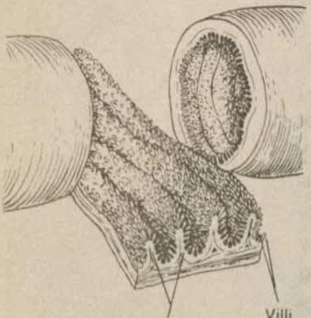


Figure 29.5 A section of the small intestine opened to reveal the folds of the inner wall and the lining covered with villi.

We are being a bit premature in describing absorption of nutrients. The process does occur in the small intestine for the most part, but only after two other organs, the pancreas and the liver, have made their contributions to the digestive process.

*It is interesting that nearly all human babies have the enzyme lactase but most adults do not. If that statement seems strange to you, then you are probably a Northern European or are of Northern European descent. People who have had their origins in Northern Europe comprise the principal populations—a definite minority—whose adults possess lactase. People who lack the enzyme get sick from drinking milk, due to the buildup of indigestible lactose. When milk is cooked or fermented, lactose is hydrolyzed. Thus, cheese, yogurt, or cooked food containing milk may present no problem to those deficient in lactase. Food sent to developing nations through foreign aid programs often included dried milk. And we never knew—until 1972—why the people of those countries didn't appreciate it.

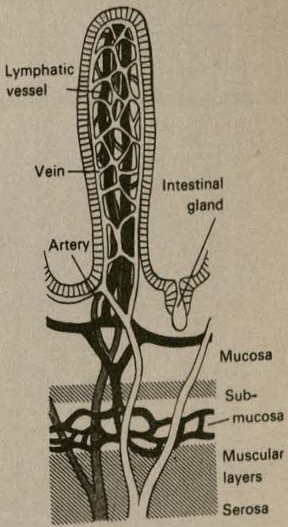


Figure 29.6 Diagram of one of the intestinal villi. Each villus contains arteries, veins, and lymphatic vessels.

29.5 Pancreatic Juice: The Finishing Touch

The pancreas is a large organ lying just below the stomach (see **figure 29.2**). It produces two kinds of secretions. One kind includes insulin, a hormone of protein nature which is emptied into the bloodstream, where it influences carbohydrate metabolism (chapter 30). The other, called pancreatic juice, passes through the pancreatic duct into the duodenum.

Pancreatic juice is rich in bicarbonate and hence is slightly alkaline, having a pH of from 7.7 to 8.0. When highly acidic chyme from the stomach reaches the duodenum, the intestinal cells release a hormone called *secretin.* This hormone reaches the pancreas through the circulatory system. It stimulates the secretion of pancreatic juice.

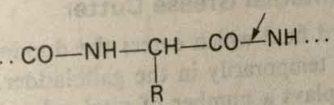
The pancreas produces enzymes for the hydrolysis of all three major food types. Three proteolytic enzymes are formed in the pancreas as proenzymes. Trypsinogen is converted to trypsin by the intestinal enzyme enterokinase (section 29.4). Trypsin, in turn, converts the pancreatic proenzymes *chymotrypsinogen* and *procarboxypeptidase* to *chymotrypsin* and *carboxypeptidase*, respectively.

$$\text{Trypsinogen} \xrightarrow{\text{enterokinase}} \text{trypsin}$$

$$\text{Chymotrypsinogen} \xrightarrow{\text{trypsin}} \text{chymotrypsin}$$

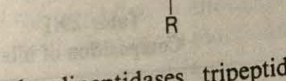
$$\text{Procarboxypeptidase} \xrightarrow{\text{trypsin}} \text{carboxypeptidase}$$

Each active enzyme works on a particular type of peptide linkage. Trypsin splits bonds of the type



$$\ldots\text{CO—NH—}\underset{\substack{| \\ \text{R}}}{\text{CH}}\text{—CO}\overset{\swarrow}{\text{—}}\text{NH}\ldots$$

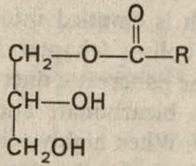
where R represents a group that makes the amino acid arginine or lysine. Chymotrypsin acts similarly when R is such that the amino acid residue is tyrosine or phenylalanine. Carboxypeptidase lops off the terminal amino acid located at the carboxyl end of the peptide chain.



$$\ldots\text{CO}\overset{\swarrow}{\text{—}}\text{NH—}\underset{\substack{| \\ \text{R}}}{\text{CH}}\text{—COO}^-$$

These enzymes, with the dipeptidases, tripeptidases, and aminopeptidases from the intestinal mucosa, complete the job of protein digestion. The free amino acids are absorbed as rapidly as they are formed. The absorption involves active transport through cell membranes and requires energy. This energy is obtained by oxidative metabolism in the cells. Absorbed amino acids are ready to be incorporated into new protein or to be converted and used for energy (chapter 32).

Pancreatic juice also contains a lipase sometimes called *steapsin.* Pancreatic lipase catalyzes the hydrolysis of fats to monoglycerides and fatty acids. A monoglyceride is a molecule in which glycerol is esterified with only one fatty acid.



$$\begin{array}{l} CH_2-O-\overset{O}{\overset{\|}{C}}-R \\ CH-OH \\ CH_2OH \end{array}$$

These components are absorbed and rapidly converted back to triglycerides. There is some evidence that the conversion back to triglycerides occurs during the absorption process. In any case, the digested lipids are absorbed by the villi lining the intestine and enter the lymphatic capillary. In this respect, the absorption of lipid differs from that of the other nutrients, which are absorbed directly into the blood. The fats, too, reach the blood, but only after traveling through the lymphatic network.

The hydrolysis of fats is extremely slow without the emulsifying action of bile salts (section 29.6).

Carbohydrate digestion by pancreatic juice involves the action of an α-amylase. This enzyme acts on the starch which escaped degradation in the mouth and upon the partially degraded dextrins produced by salivary amylase. Pancreatic amylase completes the breakdown of starch, giving maltose (87%) and some glucose (13%). The maltose is then cleaved by intestinal maltase to glucose (section 29.4).

29.6 Bile: An Internal Grease Cutter

Bile, the third fluid which enters the duodenum, is formed in the liver and then stored temporarily in the gallbladder. Bile contains no digestive enzymes, yet it plays a number of vital roles. The composition of typical bile is given in **table 29.1.**

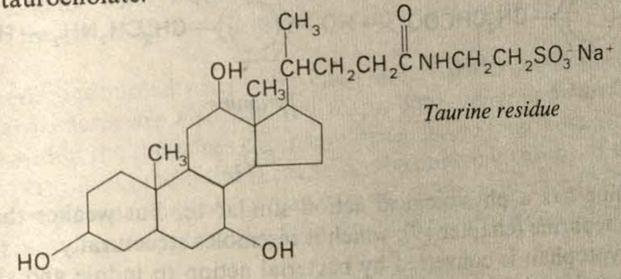
A normal adult produces 500 to 600 ml of bile each day. The fluid is slightly alkaline, with a pH of between 7 and 8. When food enters the duodenum, a hormone called cholecystokinin is released and enters the bloodstream. This hormone causes the gallbladder to empty its contents through

Table 29.1
Composition of bile

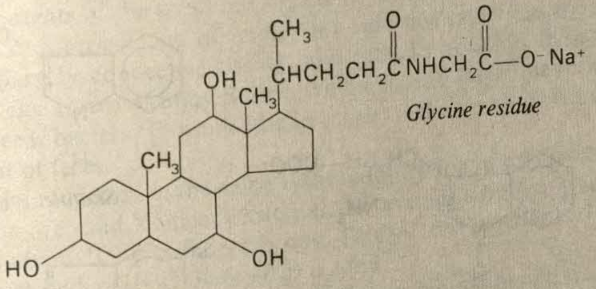
Component	*Percentage*
Water	97
Bile salts	0.7
Inorganic salts	0.7
Bile pigments	0.2
Fatty acids	0.15
Lecithin	0.1
Fat	0.1
Cholesterol	0.06

the gall duct into the duodenum. This alkaline fluid, along with the pancreatic juice, helps neutralize the acidic chyme from the stomach, providing a favorable environment for the enzymes that act in the intestine. As each load of chyme is neutralized, the stomach releases a new portion into the duodenum.

Lipids are by definition insoluble in water. The digestive juices are aqueous solutions. To bring the lipids into contact with the enzymes dissolved in the digestive juices, it is necessary to emulsify the fats. This is done by the bile salts. The principal bile salts are sodium glycocholate and sodium taurocholate.



Sodium taurocholate



Sodium glycocholate

(Taurine is an aminosulfonic acid with the formula $H_2NCH_2CH_2SO_3H$). The bile salts act in much the same way that soap does (chapter 23). They break down large fat globules into smaller ones and keep the smaller globules suspended in the aqueous digestive medium. The greatly increased surface area of the fat particles and the opportunity afforded for more intimate contact with the lipase enzymes results in a much more rapid digestion of the fats.

Bile salts also aid in the absorption of fat-soluble vitamins and cholesterol. The bile serves as a route for the excretion of drugs, end products from the breakdown of hemoglobin (section 28.6), and heavy metal ions.

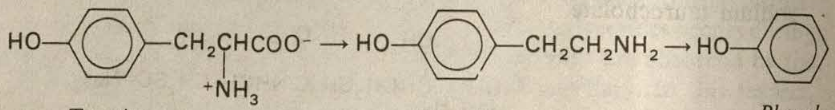
On occasion, cholesterol may precipitate in the gallbladder as *gallstones*. These may be exceedingly painful, making it necessary to remove the gallbladder.

29.7 Bacterial Action in Our Intestines

Soon after a child is born, bacteria invade its digestive tract. Thriving colonies of bacteria are established, mainly in the colon (large intestine) but also in the small intestine. Most of these bacteria are harmless. Many are beneficial. Bacteria in ruminants (grazing animals) break down cellulose, providing nourishment for their hosts as well as for themselves.

Certain bacteria act on carbohydrates in the intestine to form organic acids and gases such as methane, carbon dioxide, and hydrogen. Action of intestinal bacteria on proteins produces amines, organic acids, phenols, and ammonia. Sulfur-containing amino acids yield thiols and hydrogen sulfide.

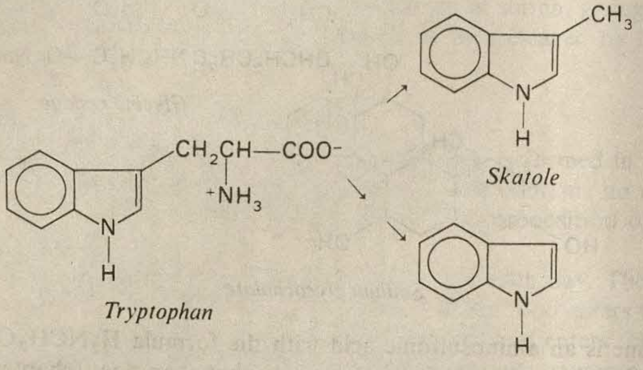
Let's look at a few specific cases. Tyrosine is converted to tyramine, and eventually to phenol, by bacterial action.



Tyrosine *Tyramine* + CO_2 *Phenol*

Tyramine has a physiological action similar to, but weaker than, that of norepinephrine (chapter 19), which it resembles structurally.

Tryptophan is converted by bacterial action to indole and skatole, two compounds largely responsible for the characteristic odor of feces.

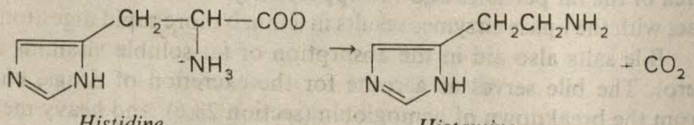


Skatole

Tryptophan

Indole

Histidine is decarboxylated by bacterial action to histamine.



Histidine *Histamine*

Histidine is a powerful vasodilator. It is most likely involved in stimulating the flow of gastric juice (section 29.3). Its complete role in the body is probably still unknown. Histamine is sometimes used in medicine. As little as 1 μg by injection causes a pronounced drop in blood pressure, by dilating the blood vessels.

Lysine and arginine, basic amino acids, are decarboxylated by bacterial action to cadaverine and putrescine, respectively.

$H_2N—CH_2CH_2CH_2CH_2CH_2—NH_2$

Cadaverine

$H_2N—CH_2CH_2CH_2CH_2—NH_2$

Putrescine

These compounds have odors as foul as their names imply. They are also toxic, but not in the amounts usually found.

The organic acids formed by bacterial action stimulate the muscular action of the colon. If formed in large amounts, these acids produce a laxative effect.

Bacteria undoubtedly act upon many other substances in the intestines. Intestinal bacteria are also believed to produce the vitamin biotin. While bacteria within the intestines can prove beneficial to their host, their release into the peritoneal (abdominal) cavity can be quite dangerous. If the gastrointestinal tract is perforated (as may happen with certain ulcers), the bacteria released may cause a potentially fatal generalized infection, peritonitis.

29.8 Feces: Formation and Composition

The contents of the small intestine enter the colon in a semiliquid state. The solid portion consists of undigested carbohydrates (largely cellulose), proteins (largely connective tissue), and fats. In addition there are dead mucosal cells, traces of unused digestive fluids, and large quantities of bacteria. Indeed, bacteria (both dead and living) make up about a third of the dry weight of feces.

The main function of the colon is the reabsorption of water, which leaves behind a more solid, compact material. An average adult on a normal diet produces about 100 g of feces per day. This material is 60% to 70% water, and the remainder (about 30 to 40 g) is solid.

The normal brown color of feces is due to bilifuscins, produced by the bacterial reduction of bilirubin (chapter 28). Abnormal colors sometimes indicate pathological conditions. Black, tarry stools indicate bleeding in the upper digestive tract. The color is due to methemoglobin, an oxidation product of hemoglobin. Blood in the stool which is still red indicates bleeding in the lower part of the tract.

Stools the color of clay indicate that little or no bile is entering the digestive tract. Such a condition indicates that an obstruction, such as a gallstone, is blocking the flow of bile. This condition, in which the patient's skin turns yellow due to a buildup of bilirubin, is called obstructive jaundice.

Certain drugs and foods also color the feces. Iron and bismuth compounds turn the stool black due to the formation of sulfides. Rhubarb may cause a yellowish stool.

Material may remain in the colon for a day or longer. Normal bowel movements may occur as often as three times a day or as seldom as once every 3 days. Laxatives, despite much advertising on television, are seldom needed. There is evidence, however, that the highly processed, low-bulk diet of the average person in the developed countries is harmful. The high-bulk diet, containing lots of fibers, peels, seeds, and the like, of more "primitive" people may be better. Such diets yield robust stools, with low retention times in the colon. Cancer of the colon has been correlated with the low-bulk diets of people in the industrialized nations.

Problems

1. Give the location of action and the function of each digestive enzyme.
   - a. salivary amylase (ptyalin)
   - b. pepsin
   - c. trypsin
   - d. chymotrypsin
   - e. pancreatic amylase
   - f. sucrase
   - g. lactase
   - h. pancreatic lipase (steapsin)
   - i. carboxypeptidase
   - j. dipeptidase
   - k. enterokinase
   - l. nucleotidase
   - m. maltase
2. What is mucin? What is its function in saliva?
3. What is pepsinogen? How is it converted to pepsin?
4. What is intrinsic factor?
5. What ion causes pancreatic juice to be slightly alkaline?
6. If the optimum pH for an enzyme were 8, would it be more active in the stomach or in the small intestine?
7. How is chyme neutralized in the duodenum?
8. Why would an episode of severe vomiting lead to a decrease in the chloride ion concentration in various body fluids?
9. Describe the emulsifying action of bile salts. What function does emulsification serve?
10. What are gallstones? What is their chief chemical component?
11. What are the end products of each of the following?
    - a. carbohydrate digestion
    - b. fat digestion
    - c. protein digestion
12. Which class of foods is absorbed into the lymph instead of directly into the blood?
13. What causes the flow of each of the following?
    - a. gastric juices
    - b. pancreatic juice
    - c. bile
14. What is the composition of feces?
15. What is indicated by a black, tarry stool? By a clay-colored stool?
16. Describe three functions of bacteria in the digestive tract. Is there a difference between bacteria in the digestive tract and in the abdominal cavity? Explain.

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chapter 30

Carbohydrate Metabolism

Green plants, using energy from the sun, make carbohydrates by a process called *photosynthesis*. What photosynthesis has joined together, the digestive and metabolic processes take apart. Plants make glucose; plant and animal cells "burn" glucose for energy. As far as the net process is concerned, this "burning" is the reverse of photosynthesis.

$$C_6H_{12}O_6 + 6\ O_2 \underset{\text{photosynthesis}}{\overset{\text{"burning"}}{\rightleftharpoons}} 6\ CO_2 + 6\ H_2O + 673\ \text{kcal/mole}$$

If we burned 1 mole (180 g) of glucose in the laboratory we would get 673 kcal of heat—enough to convert 1 ℓ of water to steam. We need that energy to keep warm, but we need other forms of energy as well. We need mechanical energy to move muscle fibers and electrical energy to carry messages along nerves. Our bodies must be able to release energy slowly, as needed, and not in sudden, large bursts that would be destructive to cells.

We take in carbohydrates mainly as starch but also as disaccharides or even monosaccharides. We saw in chapter 29 how starches and disaccharides are broken down by the digestive juices into the monosaccharides glucose, fructose, and galactose. These are absorbed directly into the bloodstream through capillaries in the villi, the fingerlike projections on the walls of the small intestine.

Once absorbed into the bloodstream, the monosaccharides are interconverted and enter a variety of different reaction schemes called *pathways*. Some pathways are designed to liberate the energy stored in the monosaccharides. Others yield starchlike products which can be stored until the energy they contain is needed. Plants offer another pathway through which glucose can be condensed into cellulose for the construction of cell walls. Incorporated into some of these schemes are cyclic pathways. The cycles are like merry-go-rounds, with passengers getting on and off. The "passengers" on these "energy-go-rounds," however, are changed as they ride. And the energy-go-round is a producer, not a consumer, of energy.

We shall travel several of these different pathways in this chapter. We shall learn how our cells get the energy we need for work and play, for breathing, and even for thinking.

30.1 Sugar in the Blood: Too Much, Too Little, and Just Right

What happens to the monosaccharides after they leave the digestive tract and enter the bloodstream? First they are carried to the liver. There they are phosphorylated. The fructose product, fructose 6-phosphate, may immediately enter the *glycolysis* pathway (section 30.4), which provides energy to the cell. The fructose product can also enter a series of reversible reactions in which it and other phosphorylated monosaccharides are interconverted (**figure 30.1**). Thus, all of the monosaccharides can ultimately enter the glycolysis pathway through the fructose 6-phosphate intermediate. Simi-

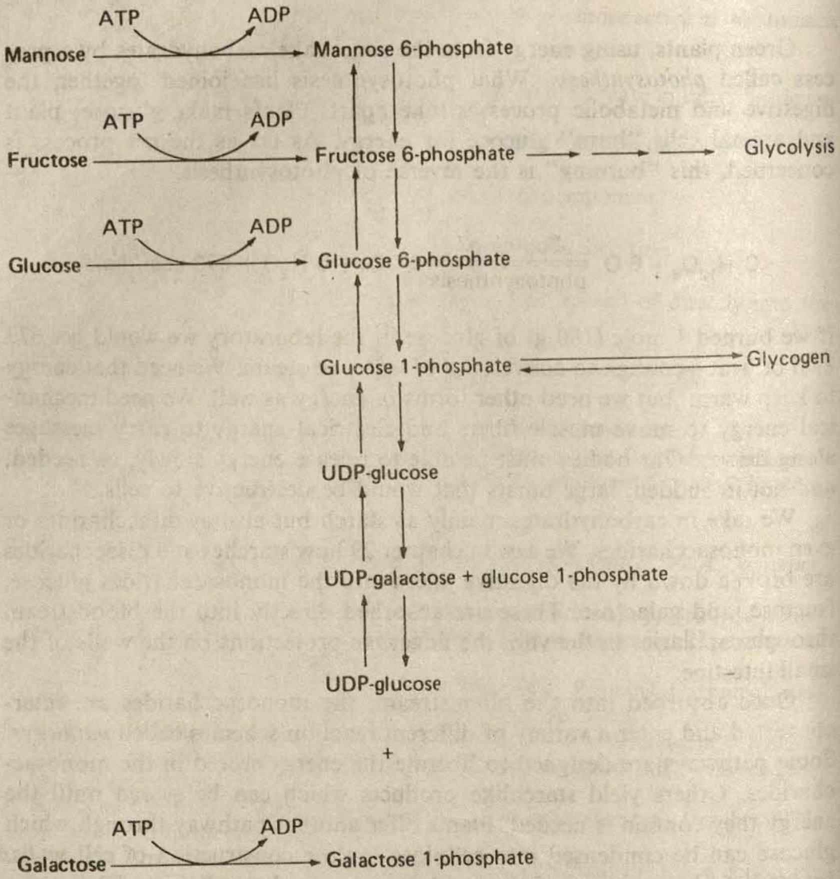

Figure 30.1 Schematic diagram for the interconversion of hexose sugars. UDP is uridine diphosphate, a nucleoside derivative which serves as a carrier of sugar molecules.

Of the various interconversions shown in **figure 30.1,** that in which galactose is converted to a glucose derivative is of particular interest. Some babies are born lacking an enzyme necessary for this conversion. This condition, called *galactosemia,* is hereditary. Infants with galactosemia cannot tolerate milk, because the hydrolysis of milk sugar (lactose) to galactose and glucose in the intestine results in the buildup of galactose and eventually in a lack of appetite, weight loss, diarrhea, and jaundice. These infants may die of cirrhosis of the liver. Milk and other sources of galactose must be replaced in the diet of an infant with galactosemia.

larly, all the monosaccharides can be converted to glucose 1-phosphate. This intermediate can, in turn, be converted to glycogen, a compound which serves as an energy reserve in animals (section 30.3).

The sugar in the blood is mainly glucose. Normal concentrations for a fasting person range from 60 to 100 mg of glucose per 100 ml of blood. There is considerable controversy over just what "normal" levels should be, with some medical professionals accepting lower or higher values than those we have given as normal. After a meal rich in carbohydrates, the level may be temporarily much higher. The condition of high blood sugar is called *hyperglycemia.* After severe starvation or vigorous exercise, the blood sugar concentration may fall below normal, leading to the condition called *hypoglycemia.** Neither condition, if temporary, is necessarily pathological, because the body has several methods of regulating the level of glucose in the blood.

We saw in chapter 28 that the kidneys may excrete excess glucose. The renal threshold value is fairly high, however, ranging from 150 to 170 mg of glucose per 100 ml of blood. In general, the kidneys are designed to conserve the glucose in the blood. Only when the blood glucose level goes well above "normal" will the kidneys shunt some of the glucose into the urine. The liver also helps to regulate blood glucose level by converting excess sugar to glycogen (section 30.3). Excess glucose may also be converted to fats for storage. And, of course, the glucose may be oxidized in the cells, producing energy.

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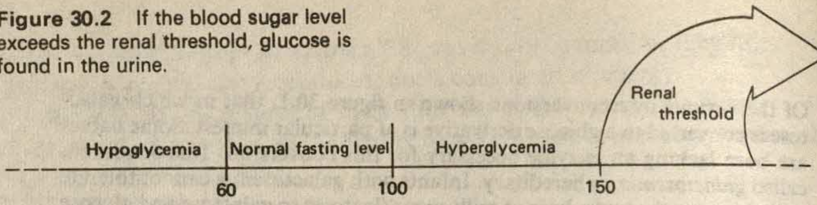
*There is a great deal of controversy regarding hypoglycemia. There are some clear-cut cases in which easily recognized symptoms are evident. These include general weakness, trembling, and rapid heartbeat. Severe cases can lead to delirium, coma, and even death. The treatment for hypoglycemia is simple. Give the patient some sugar. If the person is unconscious, glucose solution can be administered intravenously. A common cause of hypoglycemia is an overdose of insulin. Diabetics generally carry candy to counteract excess insulin. Some medical professionals contend that many of us suffer from (mild?) hypoglycemia. Some people, who are generally regarded with suspicion, attribute nearly everything that ails us to hypoglycemia. Available data do leave room for differences of opinion, and much more research is needed in this area.

Figure 30.2 If the blood sugar level exceeds the renal threshold, glucose is found in the urine.



Blood sugar level, in milligrams of glucose per 100 ml of blood

30.2 Keepers of the Gates: Hormones and Blood Sugar Levels

There are a variety of hormones that affect the blood sugar level. Perhaps the most important and certainly the best known of these is *insulin,* a protein-type hormone formed in the pancreas. Its primary structure was determined by Frederick Sanger, who won the Nobel Prize for chemistry in 1958. Insulin is made up of two chains (called A and B) cross-linked by two disulfide bonds (**figure 30.3**). Another disulfide group forms a loop in the A chain.

Insulin secretion is stimulated by a rise in the level of blood sugar. The hormone then serves to increase the rate at which tissues and organs absorb the circulating glucose for storage, oxidation, or transformation. Insulin acts by increasing the transport of glucose across cell membranes. Under its influence the glucose content of the blood is rapidly diminished. If glucose is to be stored, it is converted to glycogen in muscles and to fat in adipose (fatty) tissues. Glucose can be oxidized to carbon dioxide and water in both kinds of tissue. Insulin also causes increased glycogen storage in the liver, reducing glucose output by that organ. Although it influences carbohydrate metabolism in muscles, adipose tissue, and the liver, insulin has no effect on carbohydrate metabolism in the brain or kidneys. Insulin also exhibits some activity in amino acid metabolism and protein production.

If the pancreas is removed surgically, or if the cells which produce insulin are destroyed, the carbohydrate storage mechanisms don't work properly. The result is an increase in blood sugar level. The renal threshold is exceeded, and glucose is found in the urine. The production of large quantities of sugar-containing urine is characteristic of persons suffering from *diabetes mellitus,* the disease which results from faulty insulin production. As carbohydrate metabolism is impaired, the liver produces keto acids by the metabolism of fatty acids (chapter 31). Severe acidosis and *diabetic coma* may ensue. This condition is fatal if not reversed.

Fortunately, insulin is available as a by-product of the meat-packing industry. Since it is protein in nature, insulin cannot be administered orally. It would be deactivated by the same digestive processes which break down the protein we eat for food. It is usually injected subcutaneously. Administered at the proper level, insulin keeps carbohydrate metabolism regulated, enabling diabetics to live nearly normal lives.

The oral drugs used to control mild cases of diabetes are not protein in nature; rather, they are synthetic chemical substances such as tolbutamide (*Orinase*).

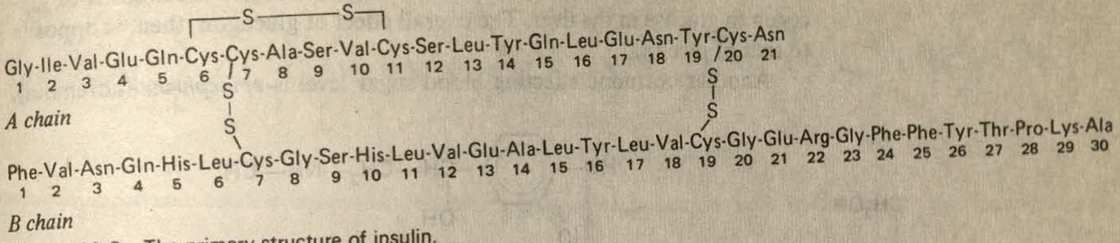
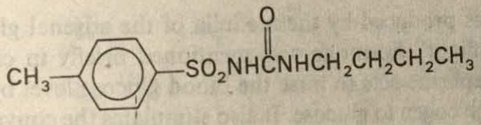

S
S
Gly-Ile-Val-Glu-Gln-Cys-Cys-Ala-Ser-Val-Cys-Ser-Leu-Tyr-Gln-Leu-Glu-Asn-Tyr-Cys-Asn
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
A chain
Phe-Val-Asn-Gln-His-Leu-Cys-Gly-Ser-His-Leu-Val-Glu-Ala-Leu-Tyr-Leu-Val-Cys-Gly-Glu-Arg-Gly-Phe-Phe-Tyr-Thr-Pro-Lys-Ala
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
B chain

Figure 30.3 The primary structure of insulin.



These compounds stimulate the release of insulin from the pancreas. Therefore, they are only effective for persons who manufacture their own insulin but who fail to release the insulin in response to increased blood sugar level. The drugs recently have been shown to increase the risk of heart disease. Their use has become rather controversial.

A *glucose tolerance test* is used to diagnose diabetes mellitus. A patient's blood glucose level is determined after a fast of several hours. Then a certain amount (25 to 100 g) of glucose is administered, and the patient's blood glucose level is measured at intervals. In normal persons, the level will rise initially but will return to normal or slightly less than normal in about 2 hours. With diabetic patients the level will be high at the start, will go even higher, and will remain at the elevated levels for several hours (**figure 30.4**).

Glucagon is another pancreatic hormone. It is a polypeptide with 29 amino acid residues.

His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-Arg-Arg- . . .

. . . Ala-Gln-Asp-Phe-Val-Gln-Try-Leu-Met-Asn-Thr

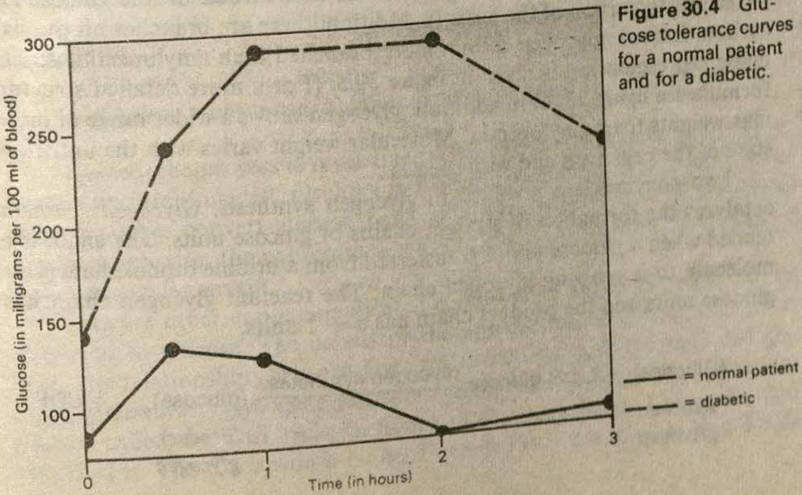
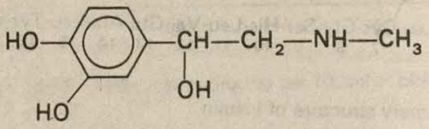


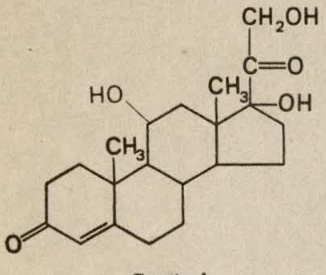
Figure 30.4 Glucose tolerance curves for a normal patient and for a diabetic.

It raises the blood sugar level by increasing the rate of breakdown of glycogen to glucose in the liver. The overall effect of glucagon, then, is opposite to that of insulin.

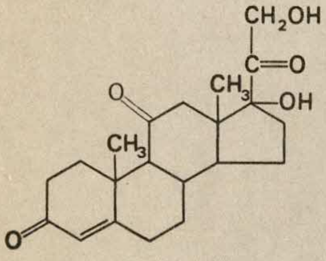
Another hormone affecting blood sugar level is *epinephrine* (adrenalin).



This hormone is produced by the medulla of the adrenal glands. Its action as a "fight or flight" hormone was mentioned briefly in chapter 19. Like glucagon, epinephrine acts to raise the blood glucose level by increasing the breakdown of glycogen to glucose. It also stimulates the conversion of muscle glycogen to lactic acid, raising the level of that metabolite in the blood. Fright may be such that enough epinephrine is secreted to raise the blood glucose level above the renal threshold. Glucose will appear in the urine. Sometimes this condition, called *emotional glycosuria,* will appear during a routine physical examination—if the examinee is sufficiently frightened.



Cortisol



Cortisone

Hormones of the adrenal cortex also affect blood sugar level. *Cortisone* and *cortisol* are two such compounds. These hormones stimulate the synthesis of glucose in the liver from amino acids. They, too, are antagonistic to insulin. The adrenocortical hormones are controlled in turn by the adrenocorticotropic hormone (ACTH). ACTH is produced in the anterior pituitary gland. Another pituitary hormone which influences the blood glucose level is the *human growth hormone*. This hormone stimulates glucagon secretion and is antagonistic to insulin.

30.3 The Energy Bank: Glycogen

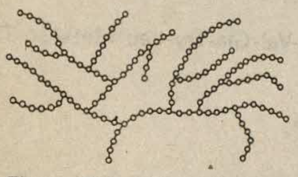


Figure 30.5 Schematic drawing of a glycogen molecule.

The structure of glycogen is much like that of amylopectin (chapter 22), the branched component of starch. Glycogen consists of a chain of glucose units, joined by an alpha linkage from the first carbon of one glucose unit to the fourth carbon of the next. In addition, there are branches off the sixth carbon. Indeed, glycogen is even more branched than amylopectin. A schematic representation is given in **figure 30.5.** (For a more detailed structural formula see **figure 22.4.**) In addition, glycogen shows a wider range of molecular weights than amylopectin. Molecular weight varies with the nutritional state of the organism and with species.

Two enzymes are involved in glycogen synthesis. *Glycogen synthetase* catalyzes the formation of straight chains of glucose units. The chain is extended when a glucose unit is transferred from a uridine diphosphate (UDP) molecule to a growing glycogen chain. The reactant glycogen chain has *n* glucose units and the product chain has *n* + 1 units.

$$\underset{\textit{Reactant glycogen}}{(\text{Glucose})_n} + \text{UDP-glucose} \xrightarrow{\text{glycogen synthetase}} \underset{\textit{Product glycogen}}{(\text{glucose})_{n+1}} + \text{UDP}$$

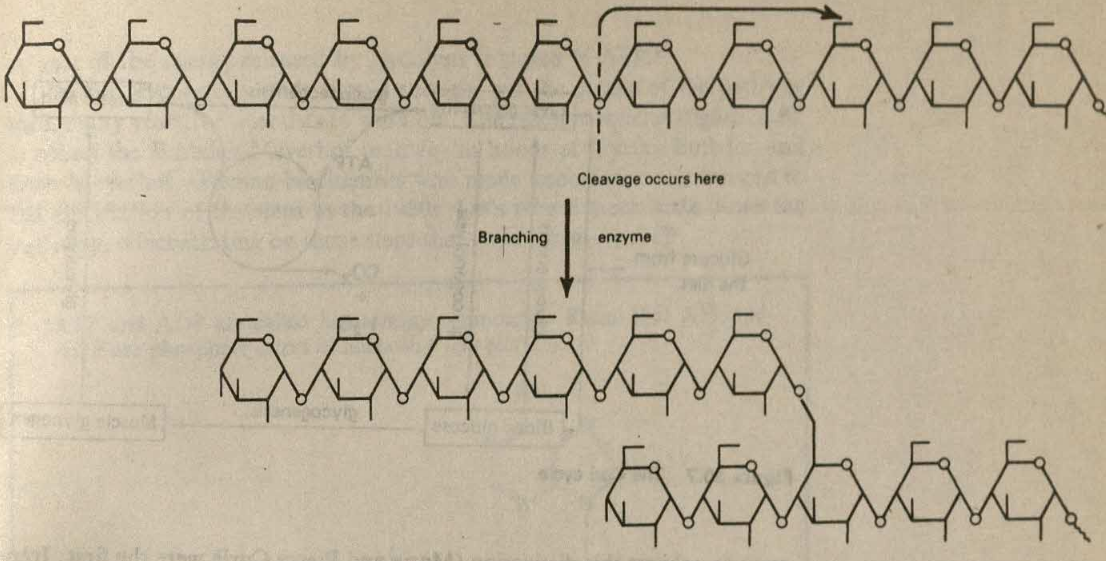


Figure 30.6 Formation of a glycogen branch.

The glycogen synthetase enzyme is not involved in the formation of the 1,6 bonds found in the branched glycogen structure. Another enzyme, called the *branching enzyme,* is responsible for breaking off a piece of the straight chain at one of the 1,4 linkages and repositioning it at the sixth carbon (**figure 30.6**).

Glycogen serves as an energy reserve in animals. Our livers normally store about 100 g of glycogen. In exceptional circumstances, as much as 400 g may be stored. Muscles also have the capability of making and storing glycogen.

When the blood sugar level drops, glycogen is converted into free glucose. Muscle glycogen releases glucose to supply energy during muscular contraction (section 30.7). In the liver, the enzyme *phosphorylase* catalyzes the reaction

$$\text{Glucose 1-phosphate} + (\text{glucose})_n \rightleftarrows (\text{glucose})_{n+1} + \text{HPO}_4^{2-}$$

As indicated, the process is reversible. When the blood glucose level drops, the equilibrium shifts left, resulting in the formation of glucose 1-phosphate. Other enzymes convert glucose 1-phosphate to free glucose. When blood glucose levels rise, the equilibrium shifts to the right, forming glycogen of higher molecular weight.

There are other, more complicated processes by which glycogen can be converted to glucose. The details of these processes need not concern us here. The relationships between glycogen formation (glycogenesis) and glycogen breakdown (glycogenolysis) are summarized in **figure 30.7.** The diagram is called the **Cori cycle,** in honor of Gerty and Carl Cori, who first described it. The Coris won a Nobel Prize in 1947, the third husband-wife

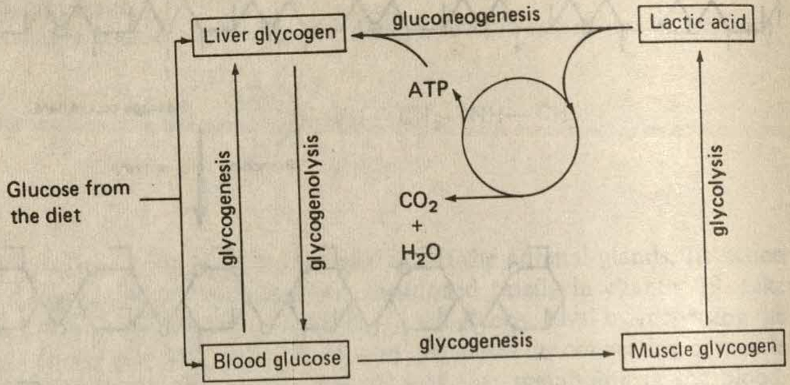


Figure 30.7 The Cori cycle.

team to achieve this distinction (Marie and Pierre Curie were the first; Irène and Frédéric Joliot-Curie, the second).

30.4 Energy without Air: Anaerobic Glycolysis

The metabolism of monosaccharides, which occurs in much the same way in most plants and animals, can take any one of several interconnected pathways. We will discuss two of those pathways: (1) anaerobic glycolysis, called the Embden-Meyerhof pathway, and (2) aerobic oxidation, variously called the Krebs cycle, the citric acid cycle, or the tricarboxylic acid cycle. Let's look first at anaerobic glycolysis.

The overall result of anaerobic glycolysis is the conversion of a glucose molecule into two molecules of lactic acid.

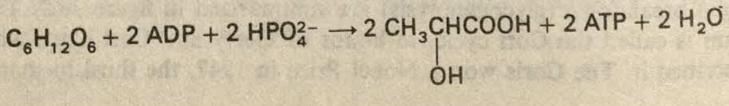
$$\underset{\textit{Glucose}}{C_6H_{12}O_6} \longrightarrow \underset{\textit{Lactic acid}}{2\ C_3H_6O_3}$$

The word *glycolysis* means "splitting of a sugar." Note that glucose is neither oxidized nor reduced in the reaction. (The oxidation number of carbon in each compound is 0.) There are, however, oxidation and reduction processes involved along the way.

Glycolysis releases energy. Part of that energy goes to convert inorganic phosphate and ADP to ATP.

$$2\ ADP + 2\ HPO_4^{2-} \longrightarrow 2\ ATP + 2\ H_2O$$

The overall process which results from the two coupled reactions can be written



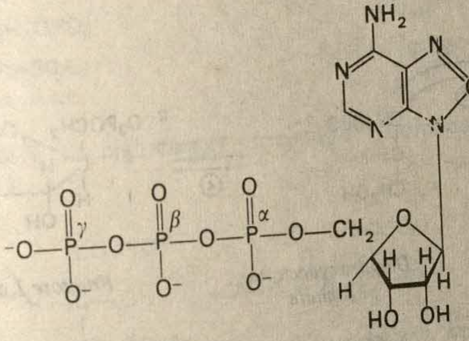
$$C_6H_{12}O_6 + 2\ ADP + 2\ HPO_4^{2-} \longrightarrow 2\ CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCOOH + 2\ ATP + 2\ H_2O$$

Glucose *Lactic acid*

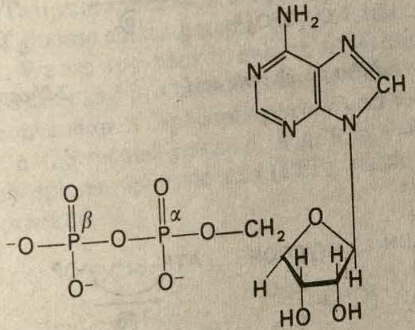
A part of the energy released by glycolysis is stored in ATP.*

So far glycolysis sounds simple enough, but the details of the pathway took many years for scientists to work out. The reaction scheme (**figure 30.8**) is called the Embden-Meyerhof pathway in honor of Gustav Embden and Otto Meyerhof, German biochemists who made important contributions to the elucidation of the steps in the 1930s. Let's take a quick walk down the pathway, concentrating on those steps that store energy in ATP.

*ATP and ADP are called high-energy compounds. Recall that ATP and ADP are phosphate esters of adenosine (chapter 25).



Adenosine triphosphate (ATP)



Adenosine diphosphate (ADP)

ATP is hydrolyzed in two steps, each of which releases considerable energy. The beta and gamma bonds are anhydride linkages. Anhydrides generally are richer in energy (more reactive) than esters. The alpha linkage is an ester linkage. Thus, AMP is not a high-energy substance. It yields considerably less energy upon hydrolysis than ATP and ADP.

ATP is the most important high-energy compound in cells. About 70% of the energy from carbohydrate metabolism is stored in ATP. The ATP in turn can provide the energy which drives metabolic reactions in cells. Indeed, the role of ATP in cellular processes is so important that ATP is called the universal energy currency of cells.

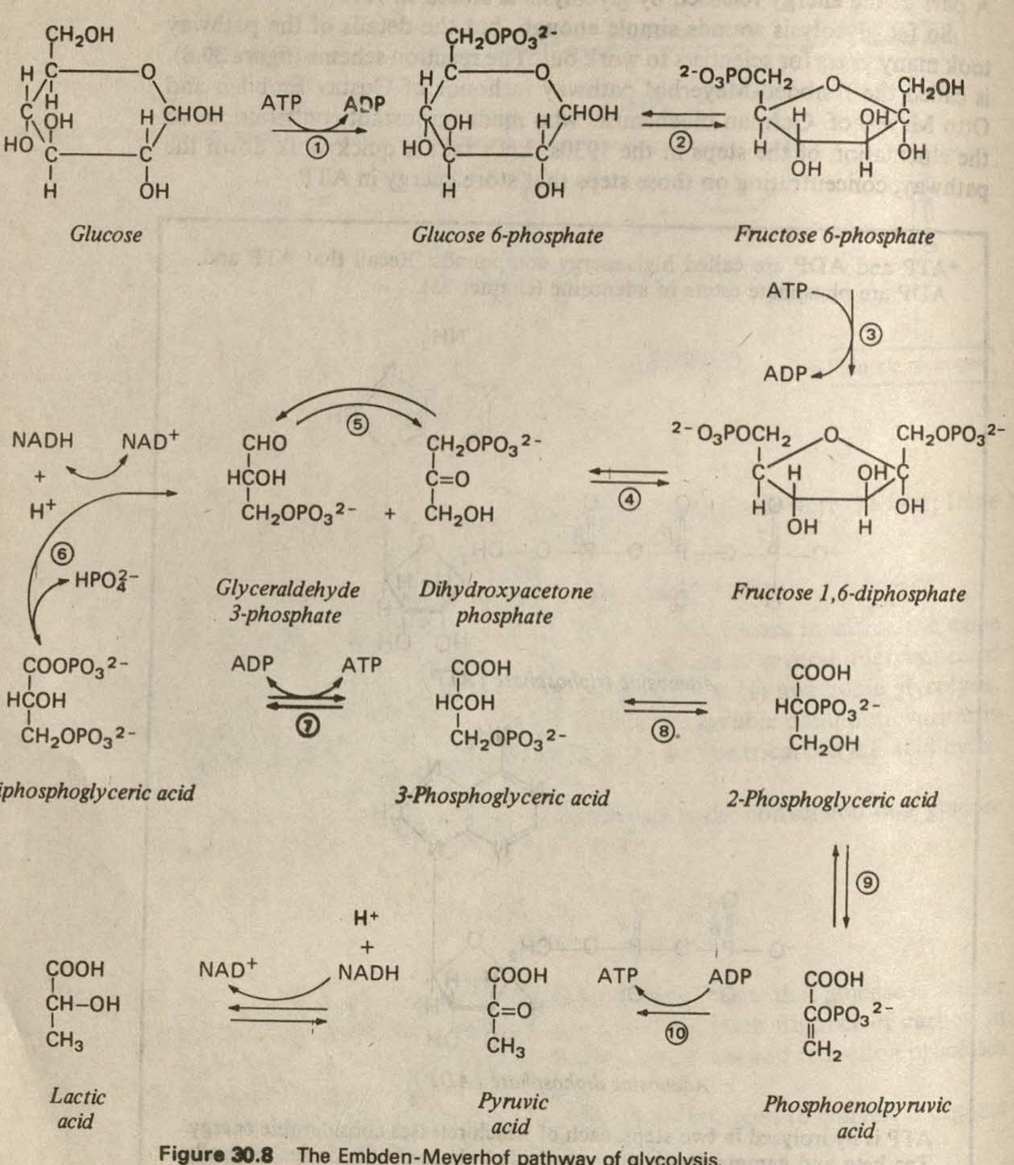
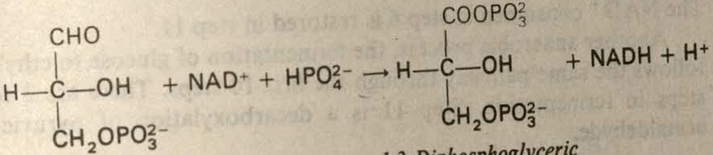


Figure 30.8 The Embden-Meyerhof pathway of glycolysis.

Notice that step 1 uses up ATP to convert glucose to glucose 6-phosphate. Step 2 involves an isomerization, probably a keto-enol shift (chapter 17). Step 3 consumes another unit of ATP to convert fructose 6-phosphate to fructose 1,6-diphosphate. Step 4 is a reversible reaction in which a six-carbon structure is broken into two three-carbon units. The reverse of this step is an aldol condensation (chapter 17). Both the forward and reverse processes are catalyzed by the enzyme *aldolase*. The two three-carbon compounds formed in step 4, glyceraldehyde 3-phosphate and dihydroxyacetone phosphate, are in equilibrium with one another. Either can be changed into the other by a keto-enol hydrogen shift (step 5).

Step 6 is an oxidative phosphorylation. NAD$^+$ oxidizes the aldehyde group of glyceraldehyde 3-phosphate to a carboxylic acid group, which is then phosphorylated to 1,3-diphosphoglyceric acid. The overall process can be summarized as

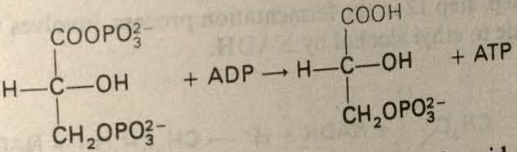


$$\begin{array}{ccc} & \text{CHO} & \\ & | & \\ \text{H}— & \text{C} & —\text{OH} \\ & | & \\ & \text{CH}_2\text{OPO}_3^{2-} & \end{array} + \text{NAD}^+ + \text{HPO}_4^{2-} \longrightarrow \begin{array}{ccc} & \text{COOPO}_3^{2} & \\ & | & \\ \text{H}— & \text{C} & —\text{OH} \\ & | & \\ & \text{CH}_2\text{OPO}_3^{2-} & \end{array} + \text{NADH} + \text{H}^+$$

Glyceraldehyde 3-phosphate

1,3-Diphosphoglyceric acid

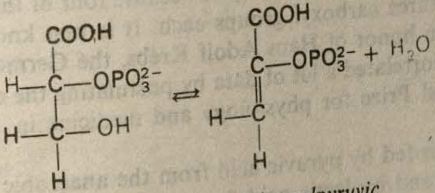
Step 7 uses the high-energy compound 1,3-diphosphoglyceric acid to produce ATP.



$$\begin{array}{ccc} & \text{COOPO}_3^{2-} & \\ & | & \\ \text{H}— & \text{C} & —\text{OH} \\ & | & \\ & \text{CH}_2\text{OPO}_3^{2-} & \end{array} + \text{ADP} \longrightarrow \begin{array}{ccc} & \text{COOH} & \\ & | & \\ \text{H}— & \text{C} & —\text{OH} \\ & | & \\ & \text{CH}_2\text{OPO}_3^{2-} & \end{array} + \text{ATP}$$

Since there are two molecules of 1,3-diphosphoglyceric acid produced for each molecule of glucose entering step 1, two molecules of ATP are produced per glucose unit. We are now back to even in ATP consumption (steps 1 and 3 each consumed one) and production (step 6 produced two).

Step 8 is a conversion of 3-phosphoglyceric acid to its isomer, which has the phosphate in the second position. Step 9 is a dehydration of the 2-phosphate to phosphoenolpyruvic acid (PEP), which, like ATP, is another high-energy compound.



$$\begin{array}{ccc} & \text{COOH} & \\ & | & \\ \text{H}— & \text{C} & —\text{OPO}_3^{2-} \\ & | & \\ \text{H}— & \text{C} & —\text{OH} \\ & | & \\ & \text{H} & \end{array} \rightleftarrows \begin{array}{ccc} & \text{COOH} & \\ & | & \\ & \text{C} & —\text{OPO}_3^{2-} \\ & \| & \\ \text{H}— & \text{C} & \\ & | & \\ & \text{H} & \end{array} + \text{H}_2\text{O}$$

2-Phosphoglyceric acid

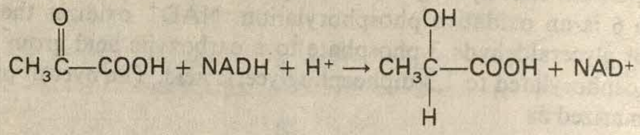
Phosphoenolpyruvic acid (PEP)

In step 10, PEP converts ADP to ATP.

$$\text{PEP} + \text{ADP} \longrightarrow \text{ATP} + \text{pyruvic acid}$$

Since there are two PEP molecules for each molecule of glucose entering the pathway, two ATPs are formed through this step. Thus, glycolysis produces a *net gain* of two ATP molecules.

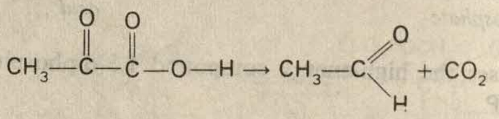
The final step of this anaerobic process is the reduction of pyruvic acid to lactic acid by NADH.



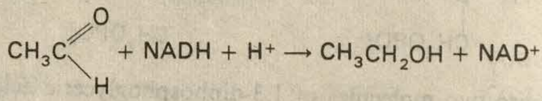
$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}\text{—}COOH + NADH + H^+ \longrightarrow CH_3\underset{\underset{\displaystyle H}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}\text{—}COOH + NAD^+$$

The NAD$^+$ consumed in step 6 is restored in step 11.

Another anaerobic process, the fermentation of glucose to ethyl alcohol, follows the same pathway through the first 10 steps. There are 2 additional steps in fermentation. Step 11 is a decarboxylation of pyruvic acid to acetaldehyde.



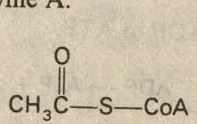
The final step, step 12 in the fermentation process, involves the reduction of acetaldehyde to ethyl alcohol by NADH.



30.5 Oxygen on Stage: Aerobic Oxidation and the Krebs Cycle

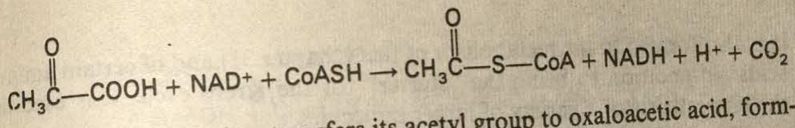
Now let's all sit back, relax, and enjoy ourselves as oxygen comes on stage to entertain us by riding the Krebs cycle. This cycle is a most unusual one. It doesn't consume energy; it produces it and does so most efficiently. The Krebs cycle masquerades under a variety of aliases. It is called the citric acid cycle because citric acid is a most important intermediate. It is also known as the tricarboxylic acid cycle because four of the intermediate compounds have three carboxyl groups each. It is best known, though, as the Krebs cycle, in honor of Hans Adolf Krebs, the German-born British biochemist who correlated a lot of data by postulating the cycle in 1937. Krebs won the Nobel Prize for physiology and medicine in 1953 in recognition of his work.

The cycle is fed by pyruvic acid from the anaerobic glycolysis pathway (section 30.4) and by lactic acid from that source or from the Cori cycle (section 30.3). Before they can enter the Krebs cycle, these compounds must be converted to acetyl coenzyme A.



$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}\text{—}S\text{—}CoA$$

The process involves several steps, with each step being catalyzed by an enzyme. The net reaction for pyruvic acid is



$$CH_3\overset{O}{\overset{\|}{C}}{-}COOH + NAD^+ + CoASH \longrightarrow CH_3\overset{O}{\overset{\|}{C}}{-}S{-}CoA + NADH + H^+ + CO_2$$

Acetyl coenzyme A then transfers its acetyl group to oxaloacetic acid, forming citric acid, and the cycle is off and rolling (**figure 30.9**).

Acetyl coenzyme A is a most versatile intermediate. Its structure is

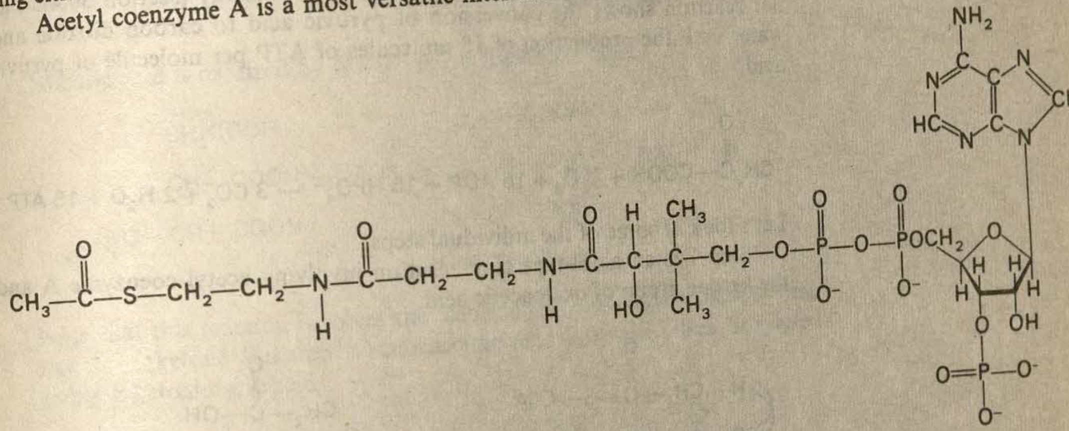
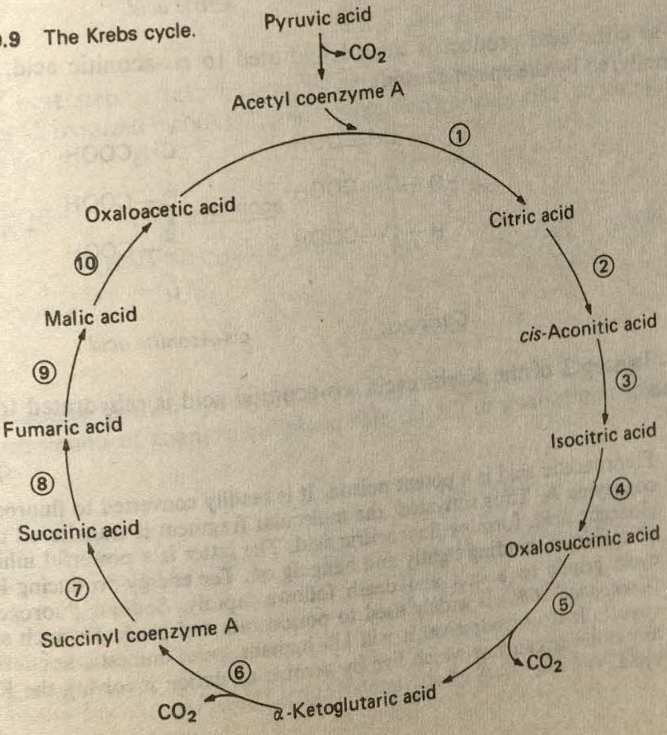
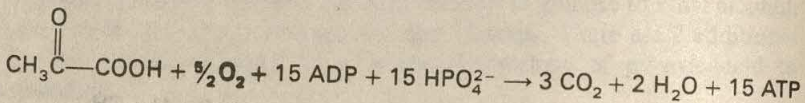


Figure 30.9 The Krebs cycle.



It is also formed in the metabolism of fats (chapter 31) and of certain amino acids. In addition to being the "starter" for the Krebs cycle, it is used in the biosynthesis of a variety of larger molecules.

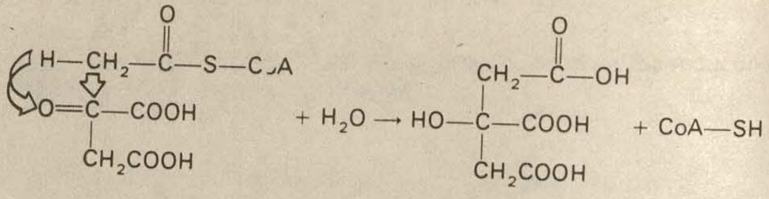
The aerobic oxidation of the Krebs cycle is much more efficient than the anaerobic processes of the Embden-Meyerhof pathway (section 30.4). The net reaction shows the conversion of pyruvic acid to carbon dioxide and water with the production of 15 molecules of ATP per molecule of pyruvic acid.



$$\mathrm{CH_3\overset{\overset{O}{\|}}{C}{-}COOH} + \tfrac{5}{2}\mathrm{O_2} + 15\,\mathrm{ADP} + 15\,\mathrm{HPO_4^{2-}} \longrightarrow 3\,\mathrm{CO_2} + 2\,\mathrm{H_2O} + 15\,\mathrm{ATP}$$

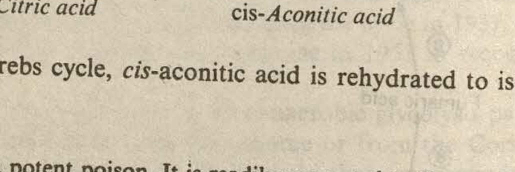
Let's look at some of the individual steps.

Step 1 is an aldol-type condensation involving acetyl coenzyme A and the ketone group of oxaloacetic acid.



Citric acid

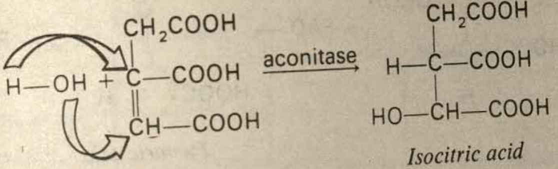
The citric acid product is then dehydrated to *cis*-aconitic acid, a reaction catalyzed by the enzyme *aconitase*.



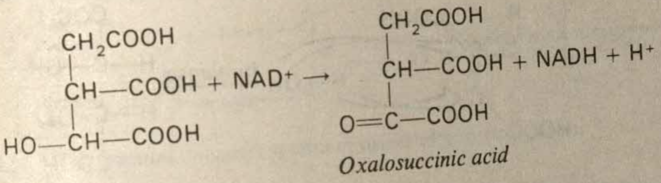
Citric acid cis-*Aconitic acid*

In step 3 of the Krebs cycle, *cis*-aconitic acid is rehydrated to isocitric acid.

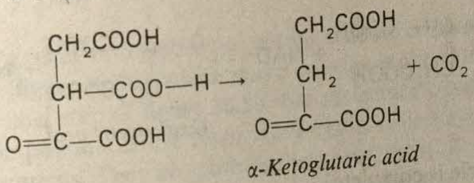
Fluoroacetic acid is a potent poison. It is readily converted to fluoroacetyl coenzyme A. Thus activated, the molecular fragment is transferred to oxaloacetic acid, forming fluorocitric acid. The latter is a powerful inhibitor of aconitase, binding tightly and hanging on. The energy-producing Krebs cycle grinds to a halt and death follows rapidly. Sodium fluoroacetate (*Compound 1080*) is widely used to poison rats and predators such as the coyote. It is not selective; it will kill humans, pets, domestic animals—or any other organisms which live by aerobic oxidation involving the Krebs cycle.



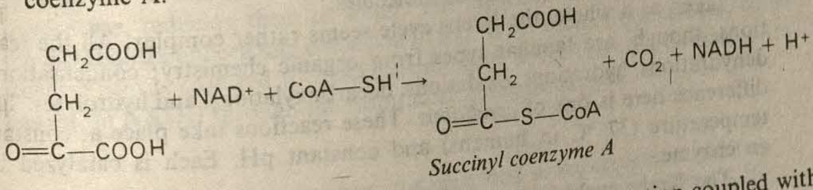
Isocitric acid is oxidized by NAD$^+$ to oxalosuccinic acid.



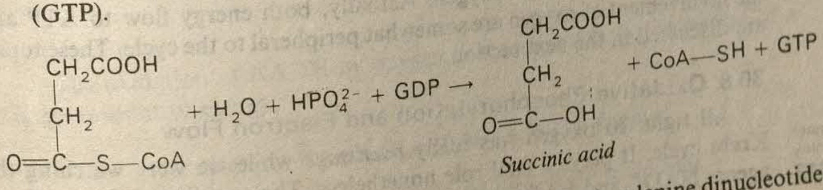
Note that this reaction involves the oxidation of a secondary alcohol function to a ketone function. Oxalosuccinic acid is readily decarboxylated, giving α-ketoglutaric acid.



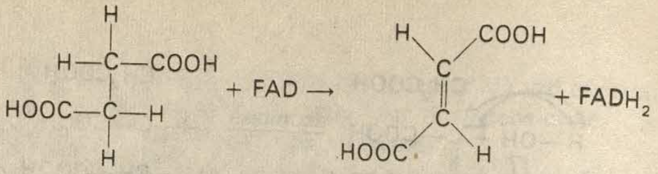
In the next step, a rather complicated one, α-ketoglutaric acid is decarboxylated, oxidized by NAD$^+$, and coupled with coenzyme A to give succinyl coenzyme A.



This thioester is then hydolyzed to succinic acid in a reaction coupled with the conversion of guanosine diphosphate (GDP) to guanosine triphosphate (GTP).

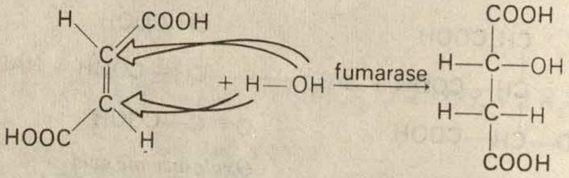


The succinic acid is oxidized (dehydrogenated) by flavin adenine dinucleotide (FAD) to fumaric acid.



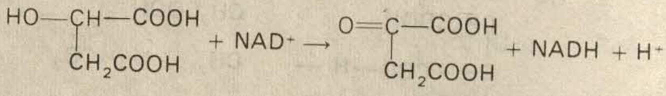
Fumaric acid

Fumaric acid is hydrated to malic acid.



Malic acid

Then the secondary alcohol group of malic acid is oxidized by NAD^+ to a ketone function in oxaloacetic acid.



$$\mathrm{HO{-}\underset{\textstyle |\atop \textstyle CH_2COOH}{CH}{-}COOH} + NAD^+ \longrightarrow \mathrm{O{=}\underset{\textstyle |\atop \textstyle CH_2COOH}{C}{-}COOH} + NADH + H^+$$

Oxaloacetic acid

And the cycle is complete!

Oxaloacetic acid can accept an acetyl group from acetyl coenzyme A, and the cycle is ready for another spin. Every time we go around the cycle, two carbons are fed into the system as acetyl coenzyme A, and two carbons are kicked out as carbon dioxide molecules.

Taken as a whole, the Krebs cycle seems rather complex. All the reactions, though, are familiar types from organic chemistry: condensations, dehydrations, hydrations, oxidations, decarboxylations, and hydrolyses. The difference here is one of *conditions*. These reactions take place at constant temperature (37 °C in humans) and constant pH. Each is catalyzed by an enzyme.

The Krebs cycle describes the fate of carbon atoms. As given in **figure 30.9,** it says little about energy flow. And although we have called the process aerobic oxidation, the oxidizing agents employed in the cycle are NAD^+ and FAD, not elemental oxygen. Actually, both energy flow to ATP and the involvement of oxygen are somewhat peripheral to the cycle. These topics are discussed in the next section.

30.6 Oxidative Phosphorylation and Electron Flow

All right, so oxygen was really *backstage* while we were watching the Krebs cycle. It plays a vital role nonetheless. The supplies of the oxidizing agents NAD^+ and FAD are limited. For the cycle to keep on turning, it is

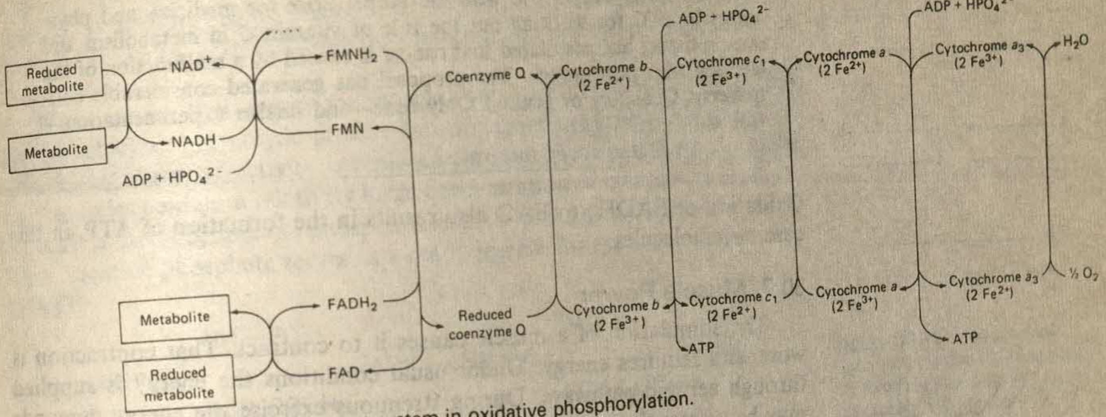


Figure 30.10 The electron transport system in oxidative phosphorylation.

necessary that NADH and $FADH_2$ be reoxidized. The ultimate oxidizing agent is oxygen, and the net equation may be written

$$NADH + H^+ + 3\,ADP + 3\,HPO_4^{2-} + \tfrac{1}{2}\,O_2 \longrightarrow NAD^+ + 3\,ATP + H_2O$$

As in most biochemical processes, the actual oxidation involves a whole series of reactions (**figure 30.10**), which make up what is called the *respiratory chain*. It is in the final step of **figure 30.10** that molecular oxygen is reduced to water. The compounds in the respiratory chain called *cytochromes* are iron-containing proteins. They are globular proteins, most of which contain one or more heme units. The iron atom may be in either the +2 or +3 oxidation state. The oxidized form (with Fe^{3+}) can accept an electron; the reduced form can donate one. Thus, electrons are transported from one cytochrome to another. Eventually, electrons are passed to molecules of oxygen gas, reducing them to water. The electrons originate ultimately in the metabolites undergoing oxidation in the Krebs cycle. For example, when isocitric acid is oxidized to oxalosuccinic acid by NAD^+, its electrons are passed *via* NADH through the respiratory chain to oxygen.

> Cyanide compounds and carbon monoxide form strong complexes with the iron atoms in the cytochromes. This inhibits action of these compounds. In sufficient concentration, the poisons shut off the respiratory chain and the cells die.

The oxidation of NADH by oxygen is accompanied by the release of a large amount of energy.

$$NADH + H^+ + \tfrac{1}{2}\,O_2 \longrightarrow NAD^+ + H_2O + \text{energy}$$

Part of this energy goes into the synthesis of three ATP molecules.

$$\text{Energy} + 3\,ADP + 3\,HPO_4^{2-} \longrightarrow 3\,ATP$$

Albert Szent-Györgyi, who won the Nobel Prize for medicine and physiology in 1937 for working out the role of vitamin C in metabolism and muscle tissue, has postulated that cancer is caused by a malfunction of the electron transport system. The proposal has generated considerable controversy. Quackery or genius? Only time—and further experimentation—will tell.

Oxidation of $FADH_2$ to FAD also results in the formation of ATP, in this case two molecules.

30.7 Muscle Power

The stimulation of a muscle causes it to contract. That contraction is work and requires energy. Under usual conditions the energy is supplied through aerobic pathways. During strenuous exercise the energy demands may be greater than can be met by aerobic oxidation alone. The respiratory system simply can't get oxygen to the muscle fast enough, and muscle metabolism shifts to an anaerobic process. In either case, muscle glycogen disappears, and there is a corresponding production of pyruvic acid. In aerobic metabolism, the pyruvic acid is fed into the Krebs cycle and oxidized to carbon dioxide. Very active muscles, operating at least partially under anaerobic conditions, reduce the pyruvic acid to lactic acid. As lactic acid builds up, the muscle's response to stimuli becomes weaker. In extreme cases there may be no response at all. In this state the muscle is described as fatigued.

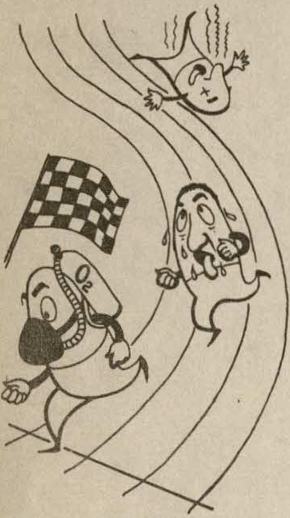


Figure 30.11 The race is to the oxygenated.

When muscles use anaerobic pathways, they incur an *oxygen debt*. It is as if the body regards oxidation as the only proper source of energy for muscular activity. Even when it can't supply oxygen fast enough for its needs and switches over to anaerobic metabolism, it does so as a temporary expedient. As soon as it can, the body will oxidize some of the resulting lactic acid back to pyruvic acid and ultimately to carbon dioxide and water. The energy released in this process will be used to convert the rest of the lactic acid back to glycogen.

When is this oxygen debt repaid? Just as soon as the very high level of muscular activity ceases. Sprinters running the 100-m dash breathe very rapidly while running. Still, only a fraction of the energy required for the muscular activity necessary for sprinting is supplied through aerobic processes. When the race is over, the sprinters continue to take in great gulps of air. This air is used to repay the oxygen debt incurred during the race. We continue to breathe hard even after we stop vigorous activity because our body chemistry is still catching up and needs some more of a critical reagent.

The immediate source of energy for muscle contraction is ATP. It is the energy stored in this molecule which is used to bring about the physical movement of muscle tissue. Two proteins, *actin* and *myosin*, play important roles in this process. Together actin and myosin form a loose complex called *actomyosin*, the contractile protein of which muscles are made (**figure 30.12**). When ATP is added to isolated actomyosin, the protein fibers contract. It seems likely the same process occurs *in vivo*, that is, in muscle tissue in living animals. Not only does myosin serve as part of the structural complex in muscles, it also acts as an enzyme for the removal of a phosphate group from ATP. Thus, it is involved in liberating the energy required for the contraction.

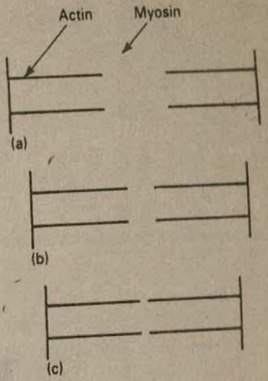
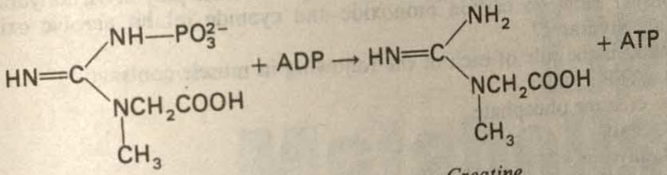


Figure 30.12 Diagram of actomyosin complex in muscle. (a) Extended muscle. (b) Resting muscle. (c) Partially contracted muscle.

When we say that energy for muscle contraction is supplied by oxidative (aerobic) and glycolytic (anaerobic) processes, we mean that the ATP used up by muscular activity is replaced through these pathways. In addition, muscles contain a relatively large concentration of creatine phosphate. As ATP is used up, creatine phosphate reacts with ADP to form more ATP. Thus, creatine phosphate serves as a ready reserve for the quick restoration of ATP.



$$HN{=}C(NH{-}PO_3^{2-})(N(CH_3)CH_2COOH) + ADP \longrightarrow HN{=}C(NH_2)(N(CH_3)CH_2COOH) + ATP$$

Creatine phosphate *Creatine*

A standard clinical test performed on individuals suspected of having suffered a myocardial infarction involves the measurement of CPK levels in the blood. CPK is *creatine phosphokinase*, the enzyme which catalyzes the phosphate transfer shown above. The heart is a muscle, and any unusual activity of this muscle (as in a "heart attack") would be accompanied by elevated CPK levels. Since other muscular activity would also increase the CPK level in the blood, the results of this test must always be interpreted most carefully.

Problems

1. Define these terms.
   a. blood sugar
   b. hypoglycemia
   c. hyperglycemia
   d. renal threshold
   e. glycolysis
   f. glycogenolysis
   g. glycogenesis
   h. glucose tolerance test
   i. galactosemia
2. What is the role of each hormone in controlling blood glucose level?
   a. insulin
   b. glucagon
   c. epinephrine
   d cortisone and cortisol
   e. human growth hormone
3. Glucose appears in the urine of a diabetic. Does glucose in the urine always indicate diabetes mellitus? Explain.
4. Why cannot insulin be taken orally?
5. In structure and purpose, how do the oral drugs such as *Orinase* differ from insulin?
6. What is the storage form of carbohydrate in the body? Where is it found? What is its structure?
7. What roles do glycogen synthetase and the branching enzyme play in glycogen formation?
8. What is the ultimate product obtained from a glucose molecule which has entered the glycolysis pathway?
9. Which step in the Embden-Meyerhof pathway involves an oxidation of a glucose metabolite? What is the oxidizing agent?

10. What critical role is played by both 1,3-diphosphoglyceric acid and phosphoenolpyruvic acid (PEP) in the Embden-Meyerhof pathway?
11. How does fermentation deviate from the Embden-Meyerhof pathway of glycolysis?
12. What is the main function of the Krebs cycle?
13. Two carbon atoms are fed into the Krebs cycle as acetyl coenzyme A. In what form are two carbon atoms removed from the cycle?
14. What are the oxidizing agents most immediately involved in the Krebs cycle?
15. What is the main function of the electron transport system of oxidative phosphorylation (the respiratory chain)? What is the ultimate oxidizing agent in this system?
16. What is a cytochrome? What role do cytochromes play in carbohydrate metabolism? How do carbon monoxide and cyanide inhibit aerobic oxidation of carbohydrates?
17. What is the role of each of the following in muscle contraction?
    a. ATP
    b. creatine phosphate
    c. actin
    d. myosin
    e. actomyosin
    f. the aerobic (oxidative) pathway of carbohydrate metabolism
    g. the anaerobic (glycolytic) pathway of carbohydrate metabolism

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chapter 31

Lipid Metabolism

In the last chapter we saw that carbohydrates are sources of energy for immediate use and reserve energy (in the form of glycogen). Carbohydrates are good sources of energy, but in many respects fats are better. In the preceding chapter, we saw that the "burning" of 1 mole (180 g) of glucose produced 673 kcal of energy, a yield of about 4 kcal/g.

$$\underset{\textit{Glucose}}{C_6H_{12}O_6} + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O + 673\ \text{kcal/mole}$$

The "burning" of 1 mole (256 g) of palmitic acid, a typical fatty acid, gives 2340 kcal of energy.

$$CH_3(CH_2)_{14}COOH + 23\,O_2 \longrightarrow 16\,CO_2 + 16\,H_2O + 2340\ \text{kcal/mole}$$

This amounts to about 9 kcal/g. Keep in mind that the "calorie" we speak of in connection with food is actually a Calorie, or kilocalorie. Thus, in nutrition books, you may find statements to the effect that fats yield 9 cal/g and carbohydrates yield 4 cal/g. Gram for gram, fats are a much richer energy source than carbohydrates. Fats are also more readily stored. The body can accommodate only a limited amount of glycogen, but considerable fat reserves can be stashed away. The glycogen reserves are mobilized more quickly, but the fat reserves last longer. Let's hear it for lipids!

In this chapter we shall look at how our bodies store and metabolize fats. We'll also consider some of the problems associated with lipid storage and metabolism. Lipids offer one of the best illustrations of an old saying. Too much of a good thing can be bad!

31.1 Blood Lipids: Normal Fasting Levels

Fats are emulsified by bile salts and are digested in the small intestine (chapter 29). Pancreatic lipase splits the fats into fatty acids, glycerol, soaps

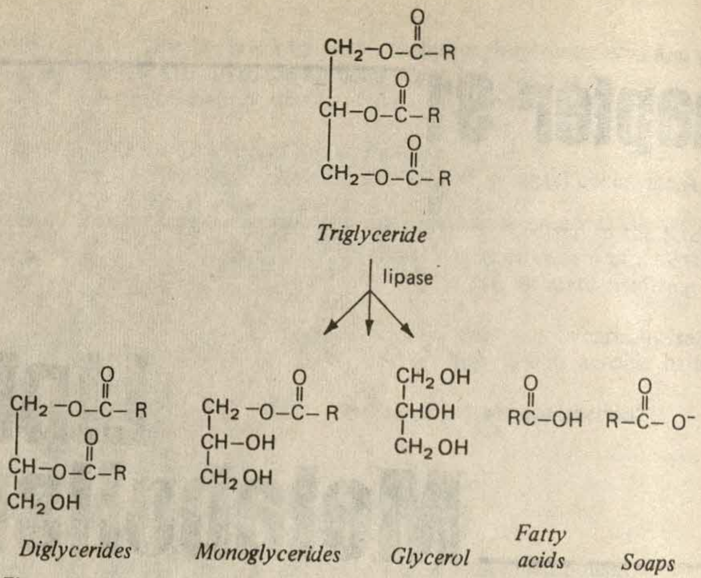


Figure 31.1 Products formed in the digestion (hydrolysis) of fats Triglyceride (fat) is hydrolyzed into diglycerides, monoglycerides, glycerol, fatty acids, and soaps.

(salts of fatty acids), and mono- and diglycerides (**figure 31.1**). As these components pass through the intestinal wall, they are reassembled as triglycerides. The reassembled products first enter the lymph system, which eventually introduces them into the blood circulation. Phospholipids are broken down and reassembled in much the same way. Some small fatty acid molecules can be directly absorbed into the bloodstream.

Lipids are, by definition, relatively insoluble in water. Since blood is an aqueous solution, fats as such are not soluble in blood. But fats can be efficiently transported by the blood if they are first complexed with water-soluble proteins in the plasma. Such complexes are called lipoproteins. Fatty acids, too, are generally complexed with proteins while being transported in the blood.

There is one advantage to the low solubility of fats, and that is that these compounds can be separated from other components of the blood by extraction with fat solvents such as benzene or chloroform. Such an extraction is always one of the first steps in any clinical procedure aimed at determining lipid levels.

The concentration of lipids in the blood changes constantly. As lipids are absorbed from the digestive tract after a meal, the level in the blood increases. As blood lipids are removed to storage or are oxidized in certain tissues, blood lipid level falls. On demand, the body can synthesize lipids from other foods or can remove already-formed lipids from storage. Both activities would result in an increase in blood lipid level. Finally, the body excretes some lipids as a normal component of feces. These excreted lipids may be in the form of fats or soaps or fatty acids. Their removal via the intestine would tend to lower the blood lipid level.

Table 31.1
Range of normal levels of lipids in blood plasma of a fasting person

Constituent	*Concentration (in milligrams per 100 ml)*
Free cholesterol	30–60
Cholesterol esters	75–150
Total cholesterol	120–250
Triglycerides	25–260
Lecithin	100–225
Sphingomyelin	10–47
Total phospholipids	150–250
Total lipids	400–700

So that the conditions under which lipid concentrations are determined are somewhat standard, lipids in the plasma are measured after fasting. This is the same procedure followed in the measurement of blood sugar levels. Typical *normal fasting levels* of lipids are given in **table 31.1.** Abnormally high levels of triglycerides and cholesterol are thought by many medical practitioners to be involved in hardening of the arteries, a condition which may lead to rupture of vessels in the brain (a stroke) or blockage of vessels in the heart (a heart attack or coronary).

31.2 Too Much Fat? Store It at the Depot

Fats are stored throughout the body. Principally, though, they are deposited in a special kind of connective tissue called *adipose tissue*. Storage places are called *fat depots*. Considerable fat is stored around vital organs such as the heart, liver, kidneys, and spleen. There it serves as a protective cushion, helping prevent injury to the organs. Fat is also stored under the skin, where it helps insulate against sudden temperature changes. The fat acts just like the insulation in the walls of a house, trapping body heat and preventing it from escaping to the surroundings. In some ways, the fatty tissue also acts like the furnace of a house. When the outside temperature drops, metabolic activity in the cells generates heat to compensate for that lost to the environment.

Some lipids, particularly phospholipids, are found as highly organized functional units of cells, for example, in bilayers which serve as cell membranes. The triglycerides in adipose tissue, on the other hand, are stored in the form of little fat globules. Each cell contains a single droplet of fat which can occupy as much as 90% of the cell's volume. The cells are all held more or less in place by the connective tissue. This adipose tissue can be quite active metabolically, and it is richly supplied with blood. When the body needs energy, the cells of the adipose tissue release fatty acids from storage. Normally this occurs only after glycogen reserves have been depleted, a few hours after eating. When the glycogen is gone, the body first uses the small amount of fat stored in the liver and then calls on the depots.

When food is taken into the body in excess of immediate needs, it is shunted to the storage areas. Fats are tucked away in the adipose tissue. Carbohydrates are converted to glycogen. When no more glycogen storage

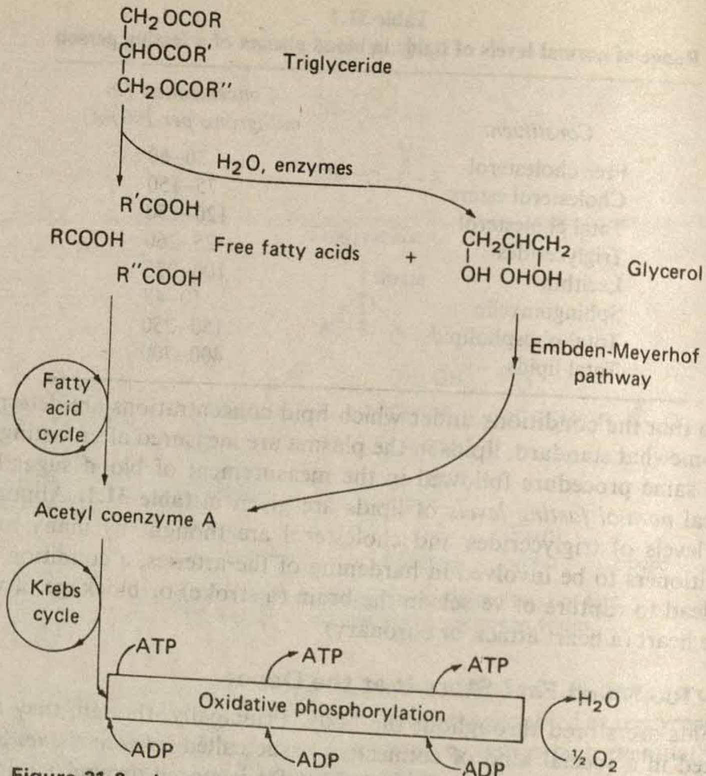
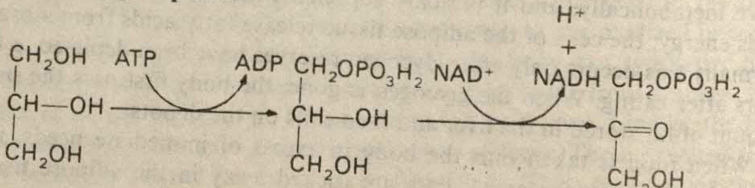


Figure 31.2 An outline showing how fat reserves (triglyceride) are used for the production of energy.

area is available, carbohydrates are converted to fats and stored in the depots. There is a continuous, dynamic change as molecules come and go from storage. If your weight is constant, there is an "equilibrium" in which the number of molecules arriving for storage is equal to the number being removed from the depot. We will discuss two situations in which there is an imbalance—obesity and starvation—in subsequent sections.

31.3 Oxidation of Fatty Acids: Two by Two

Fat reserves are metabolized in a multistep process that produces energy. The basic outline of this process is given in **figure 31.2.** First, the fat molecules are hydrolyzed to glycerol and free fatty acids. The glycerol is phosphorylated in the liver to glycerol phosphate and then is oxidized to dihydroxyacetone phosphate.



$$\begin{array}{l}CH_2OH\\|\\CH{-}OH\\|\\CH_2OH\end{array} \xrightarrow{ATP \quad ADP} \begin{array}{l}CH_2OPO_3H_2\\|\\CH{-}OH\\|\\CH_2OH\end{array} \xrightarrow{NAD^+ \quad NADH + H^+} \begin{array}{l}CH_2OPO_3H_2\\|\\C{=}O\\|\\CH_2OH\end{array}$$

Dihydroxyacetone phosphate is an intermediate in the Embden-Meyerhof

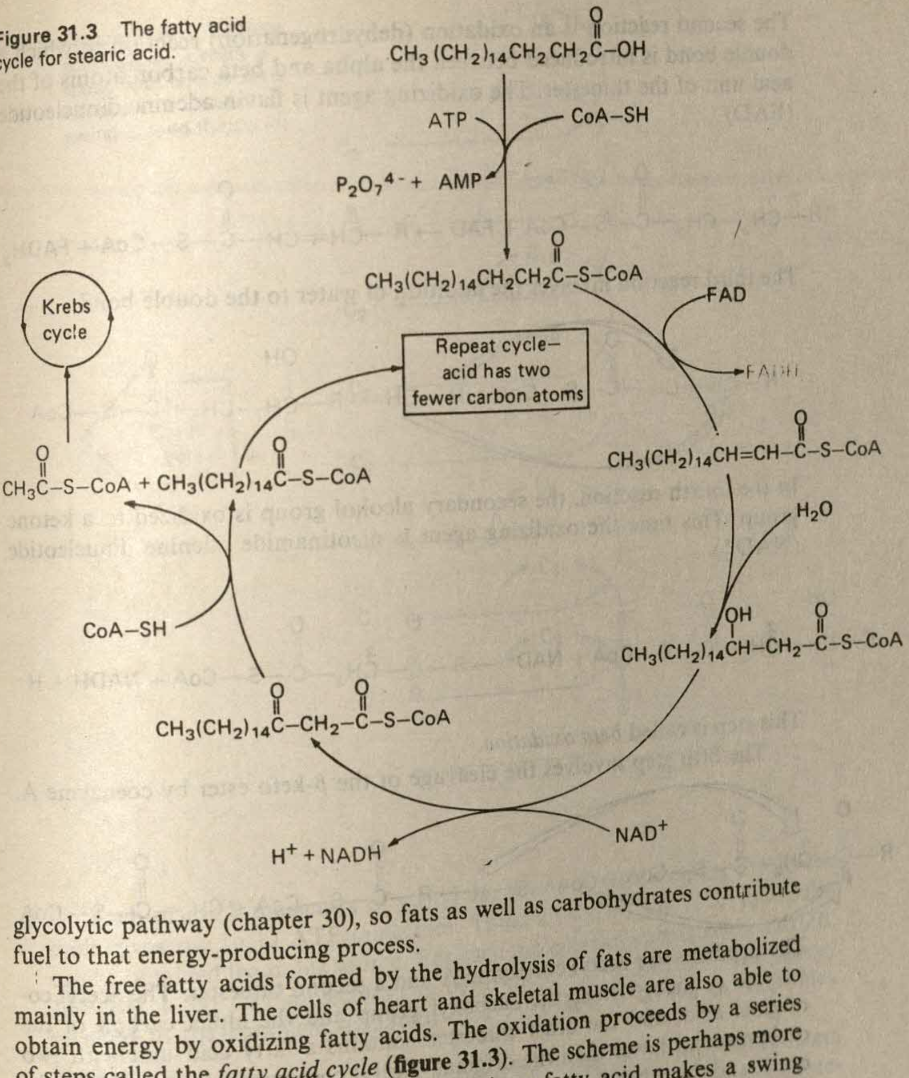
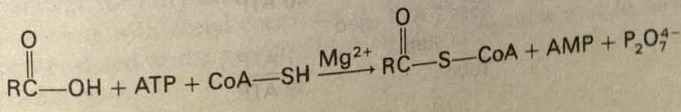

CH3(CH2)14CH2CH2C(=O)–OH
ATP
CoA–SH
P2O7 4− + AMP
CH3(CH2)14CH2CH2C(=O)–S–CoA
FAD
FADH
CH3(CH2)14CH=CH–C(=O)–S–CoA
H2O
CH3(CH2)14CH(OH)–CH2–C(=O)–S–CoA
NAD+
H+ + NADH
CH3(CH2)14C(=O)–CH2–C(=O)–S–CoA
CoA–SH
CH3C(=O)–S–CoA + CH3(CH2)14C(=O)–S–CoA
Krebs cycle
Repeat cycle— acid has two fewer carbon atoms

Figure 31.3 The fatty acid cycle for stearic acid.

glycolytic pathway (chapter 30), so fats as well as carbohydrates contribute fuel to that energy-producing process.

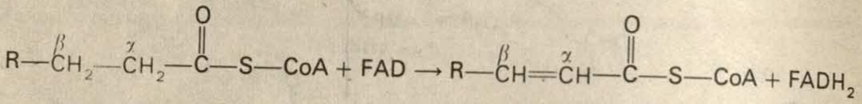
The free fatty acids formed by the hydrolysis of fats are metabolized mainly in the liver. The cells of heart and skeletal muscle are also able to obtain energy by oxidizing fatty acids. The oxidation proceeds by a series of steps called the *fatty acid cycle* (**figure 31.3**). The scheme is perhaps more appropriately called the *fatty acid spiral*. As a fatty acid makes a swing around the cycle, two carbon atoms are chopped off (**figure 31.4**) The acid entering the next swing (as its CoA thioester) is smaller by two carbon atoms. On its last swing though the cycle, the acid yields two molecules of acetyl coenzyme A.

The first reaction of the cycle involves activation of the fatty acid. The acid reacts with ATP and coenzyme A in the presence of magnesium ions to form the fatty acid thioester of coenzyme A along with adenosine monophosphate (AMP) and inorganic pyrophosphate.



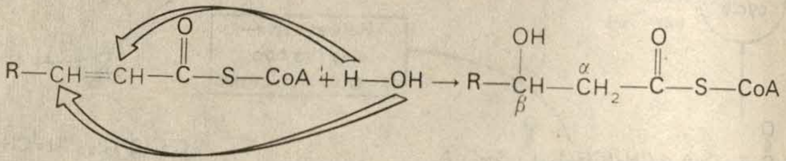
$$\mathrm{R\overset{\overset{\displaystyle O}{\|}}{C}{-}OH + ATP + CoA{-}SH \xrightarrow{Mg^{2+}} R\overset{\overset{\displaystyle O}{\|}}{C}{-}S{-}CoA + AMP + P_2O_7^{4-}}$$

The second reaction is an oxidation (dehydrogenation) reaction in which a double bond is introduced between the alpha and beta carbon atoms of the acid unit of the thioester. The oxidizing agent is flavin adenine dinucleotide (FAD).



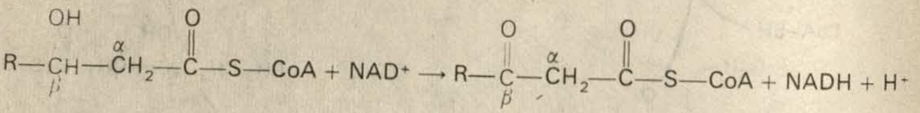
$$\mathrm{R{-}\overset{\beta}{C}H_2{-}\overset{\gamma}{C}H_2{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA + FAD \longrightarrow R{-}\overset{\beta}{C}H{=}\overset{\alpha}{C}H{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA + FADH_2}$$

The third reaction involves the addition of water to the double bond.



$$\mathrm{R{-}CH{=}CH{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA + H{-}OH \longrightarrow R{-}\underset{\beta}{\overset{OH}{\overset{|}{C}}}H{-}\overset{\alpha}{C}H_2{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA}$$

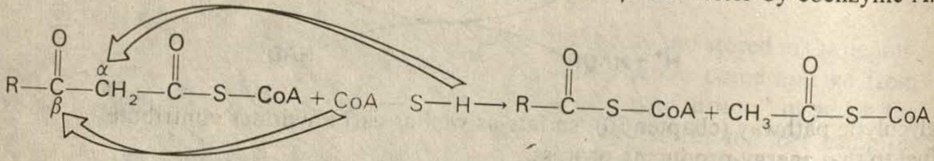
In the fourth reaction, the secondary alcohol group is oxidized to a ketone group. This time the oxidizing agent is nicotinamide adenine dinucleotide (NAD^+).



$$\mathrm{R{-}\underset{\beta}{\overset{OH}{C}}H{-}\overset{\alpha}{C}H_2{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA + NAD^+ \longrightarrow R{-}\underset{\beta}{\overset{O}{\overset{\|}{C}}}{-}\overset{\alpha}{C}H_2{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA + NADH + H^+}$$

This step is called *beta oxidation*.

The fifth step involves the cleavage of the β-keto ester by coenzyme A.



$$\mathrm{R{-}\underset{\beta}{\overset{O}{\overset{\|}{C}}}{-}\overset{\alpha}{C}H_2{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA + CoA\ \ S{-}H \longrightarrow R{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA + CH_3{-}\overset{O}{\overset{\|}{C}}{-}S{-}CoA}$$

The products are acetyl coenzyme A and a second thioester. The acetyl coenzyme A incorporates the carboxyl group and the alpha carbon of the original acid, and the other thioester contains a fatty acid unit with two carbon atoms fewer than the original. Acetyl coenzyme A enters the Krebs cycle, and the other thioester takes another spin around the fatty acid spiral.

The oxidation of stearic acid (which has 18 carbon atoms) requires eight turns of the fatty acid spiral (see **figure 31.4**) and results in the formation of 9 molecules of acetyl coenzyme A. During the oxidation, 8 molecules each of $FADH_2$ and NADH are formed. These enter the respiratory chain (chapter 30), resulting in the formation of ATP.

8 $FADH_2$	16 ATP
8 NADH	24 ATP
Subtotal	40 ATP
Less 1 ATP used in step 1	−1 ATP
Total	39 ATP

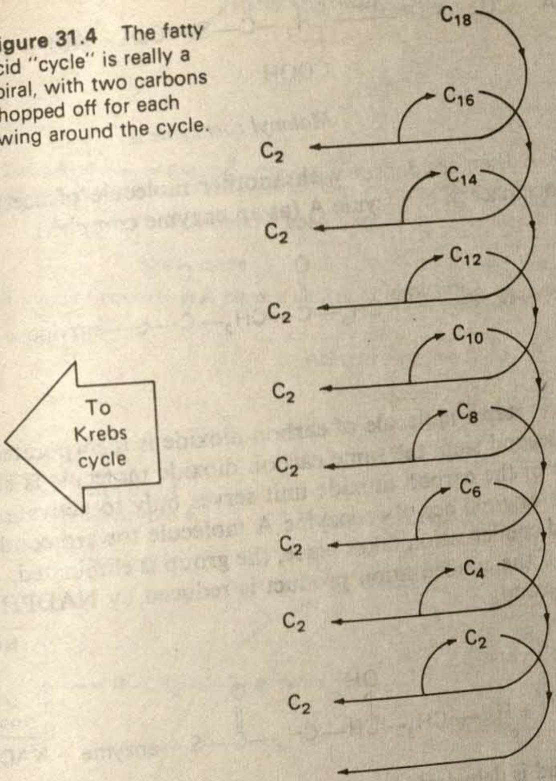


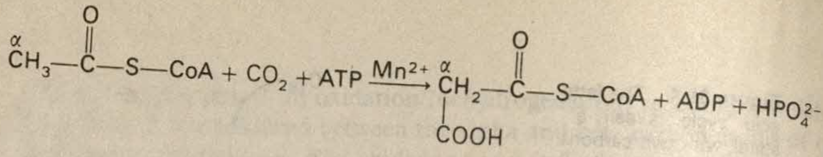
Figure 31.4 The fatty acid "cycle" is really a spiral, with two carbons chopped off for each swing around the cycle.

Each of the 9 molecules of acetyl coenzyme A which enters the Krebs cycle gives rise to 12 ATP molecules. Thus, a total of 108 ATP molecules can be obtained from this source. For each molecule of stearic acid oxidized, 147 (108 + 39) ATP molecules can be formed. About half the total energy released in the complete oxidation of a fatty acid is stored in molecules of ATP.

Not all the acetyl coenzyme A formed by oxidation of fatty acids enters the Krebs cycle. A small portion is used to *synthesize* new fatty acids (section 31.4). Some of it goes to produce cholesterol, bile salts, and other steroids (section 31.11). Still other acetyl coenzyme A is used in the formation of the "ketone bodies" (section 31.7). The various routes available to acetyl coenzyme A are summarized in **figure 31.5.**

31.4 Biosynthesis of Fatty Acids: Two by Two, Too

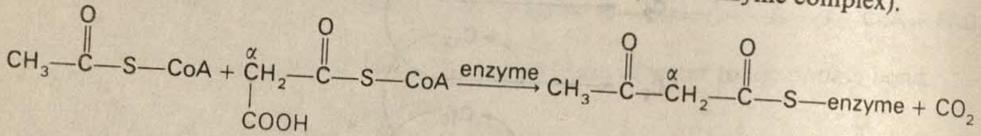
Some fatty acids are made by a reversal of the fatty acid spiral. The main pathway for fatty acid synthesis, however, is somewhat different, though it too starts with acetyl coenzyme A. In this sequence, acetyl coenzyme A is carboxylated in the presence of ATP and manganese ions to form malonyl coenzyme A.



$$\overset{\alpha}{C}H_3-\overset{\overset{O}{\|}}{C}-S-CoA + CO_2 + ATP \xrightarrow{Mn^{2+}} \underset{COOH}{\underset{|}{\overset{\alpha}{C}H_2}}-\overset{\overset{O}{\|}}{C}-S-CoA + ADP + HPO_4^{2-}$$

Malonyl coenzyme A

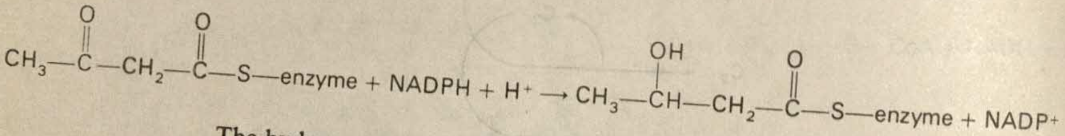
Malonyl coenzyme A then condenses with another molecule of acetyl coenzyme A to form acetoacetyl coenzyme A (as an enzyme complex).



$$CH_3-\overset{\overset{O}{\|}}{C}-S-CoA + \underset{COOH}{\underset{|}{\overset{\alpha}{C}H_2}}-\overset{\overset{O}{\|}}{C}-S-CoA \xrightarrow{enzyme} CH_3-\overset{\overset{O}{\|}}{C}-\overset{\alpha}{C}H_2-\overset{\overset{O}{\|}}{C}-S-enzyme + CO_2$$

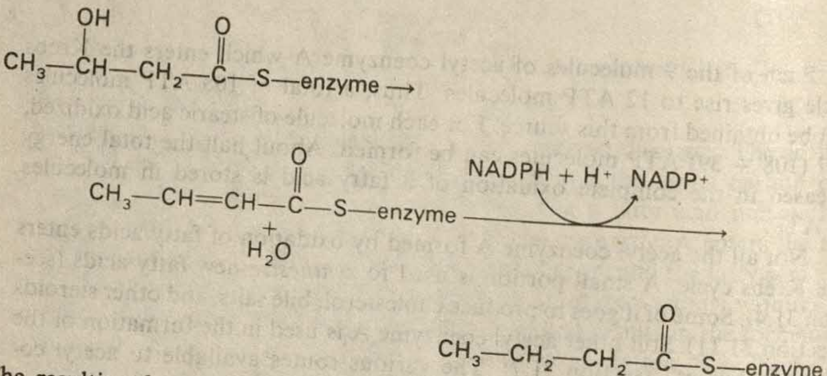
Notice that in the first step a molecule of carbon dioxide is incorporated in the product. In the second step, the same carbon dioxide molecule is eliminated. The addition of the carbon dioxide unit serves only to activate the alpha position of the original acetyl coenzyme A molecule toward condensation. As the desired condensation takes place, the group is eliminated.

The keto group of the condensation product is reduced by NADPH to a secondary alcohol group.



$$CH_3-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-S-enzyme + NADPH + H^+ \rightarrow CH_3-\overset{\overset{OH}{|}}{C}H-CH_2-\overset{\overset{O}{\|}}{C}-S-enzyme + NADP^+$$

The hydroxy compound is dehydrated, and then the unsaturated compound is reduced (hydrogenated) by NADPH.



$$\begin{gathered} CH_3-\overset{\overset{OH}{|}}{C}H-CH_2-\overset{\overset{O}{\|}}{C}-S-enzyme \rightarrow \\ \underset{\underset{H_2O}{+}}{CH_3-CH=CH-\overset{\overset{O}{\|}}{C}-S-enzyme} \xrightarrow{NADPH + H^+ \quad NADP^+} \\ CH_3-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-S-enzyme \end{gathered}$$

The resulting four-carbon product begins a second round of the cycle by undergoing condensation with another molecule of malonyl coenzyme A. Again this condensation is accompanied by the loss of a carbon dioxide molecule, so the chain length increases by only two carbon atoms. Each repetition of the cycle adds another two carbon atoms to the chain. The cycle is diagrammed in **figure 31.6.**

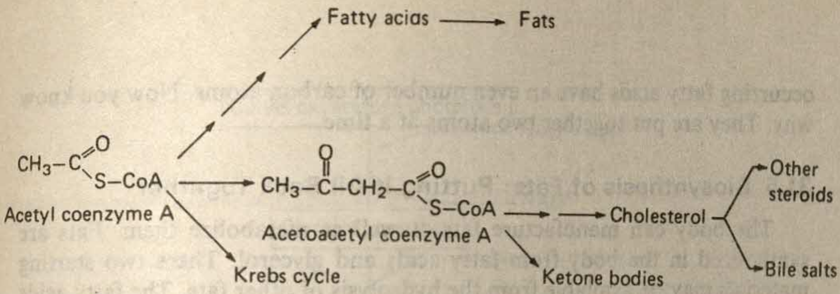


Figure 31.5 Acetyl coenzyme A plays a variety of roles in cellular chemistry.

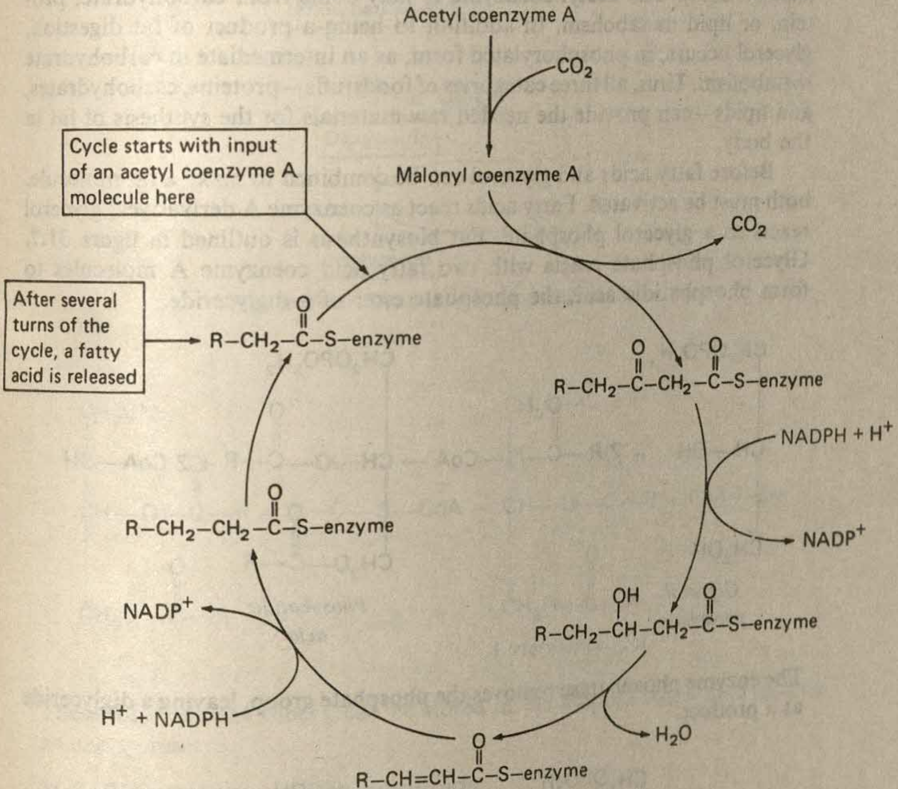

Acetyl coenzyme A
CO2
Malonyl coenzyme A
CO2
Cycle starts with input of an acetyl coenzyme A molecule here
After several turns of the cycle, a fatty acid is released
R–CH2–C(=O)–S–enzyme
R–CH2–C(=O)–CH2–C(=O)–S–enzyme
NADPH + H+
NADP+
R–CH2–CH(OH)–CH2–C(=O)–S–enzyme
H2O
R–CH=CH–C(=O)–S–enzyme
H+ + NADPH
NADP+
R–CH2–CH2–C(=O)–S–enzyme

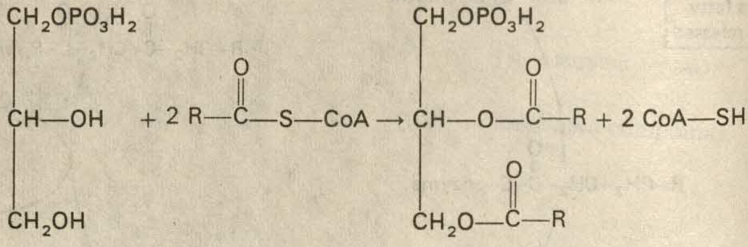
Figure 31.6 The synthesis of fatty acids.

Fatty acid synthesis through reversal of the fatty acid spiral possesses some features in common with the sequence just outlined. In the former case, acetyl coenzyme A rather than malonyl coenzyme A is directly involved in the condensation steps, and different reducing agents and enzyme systems are used. But, in general, the sequence of reactions is the same: condensation is followed by reduction, which is followed by dehydration, which is followed by another reduction. Recall from chapter 18 that most naturally occurring fatty acids have an even number of carbon atoms. Now you know why. They are put together two atoms at a time.

31.5 Biosynthesis of Fats: Putting It All Back Together

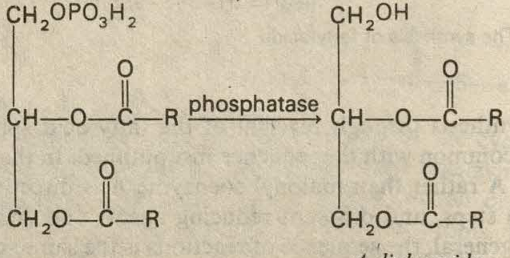
The body can manufacture fats as well as metabolize them. Fats are synthesized in the body from fatty acids and glycerol. These two starting materials may be available from the hydrolysis of other fats. The fatty acids can also be synthesized from scratch, or rather from acetyl coenzyme A (section 31.4). The acetyl coenzyme A may come from carbohydrate, protein, or lipid metabolism. In addition to being a product of fat digestion, glycerol occurs, in phosphorylated form, as an intermediate in carbohydrate metabolism. Thus, all three categories of foodstuffs—proteins, carbohydrates, and lipids—can provide the needed raw materials for the synthesis of fat in the body.

Before fatty acids and glycerol can be combined to make a fat molecule, both must be activated. Fatty acids react as coenzyme A derivatives; glycerol reacts as a glycerol phosphate. Fat biosynthesis is outlined in **figure 31.7.** Glycerol phosphate reacts with two fatty acid coenzyme A molecules to form phosphatidic acid, the phosphate ester of a diglyceride.



Glycerol phosphate *Phosphatidic acid*

The enzyme phosphatase removes the phosphate group, leaving a diglyceride as a product.



A diglyceride

The diglyceride then reacts with the coenzyme A derivative of another fatty acid, giving the triglyceride, or fat.

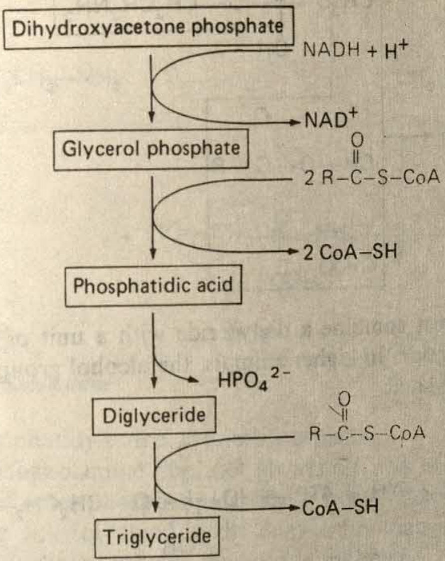
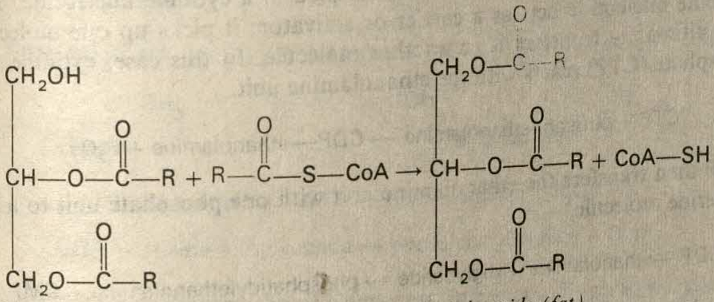


Figure 31.7 The biosynthesis of triglyceride.



A triglyceride (fat)

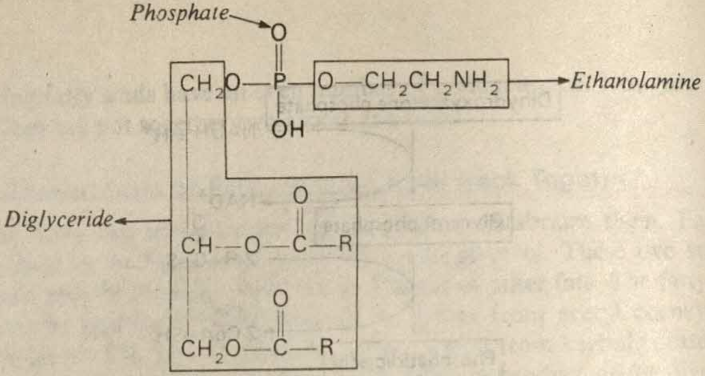
These fats, like any others, can be stored in the adipose tissue and used as an energy reserve.

31.6 Biosynthesis of Phospholipids

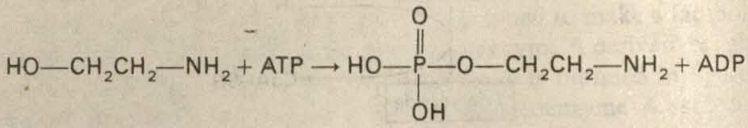
A phospholipid generally has a polar end and a nonpolar end. Phospholipids often serve to bridge the gap between the less polar fats and the highly polar aqueous body fluids. Phospholipids are involved in electron transport systems and in the movement of fats and fatty acids through the walls of the digestive tract and from the liver and fat depots to other tissues.

When eaten, phospholipids are probably digested in much the same way as other lipids. The constituent parts are then reassembled to make new phospholipids. Intermediates from fat metabolism or other sources can also be used in the synthesis of phospholipids.

Let us suppose that we want to make phosphatidylethanolamine, a cephalin (chapter 23).



Somehow we must combine a diglyceride with a unit of phosphate and a unit of ethanolamine. In higher animals, the alcohol group of ethanolamine is first phosphorylated.



$$HO—CH_2CH_2—NH_2 + ATP \longrightarrow HO—\overset{\overset{\Large O}{\|}}{\underset{\underset{\Large OH}{|}}{P}}—O—CH_2CH_2—NH_2 + ADP$$

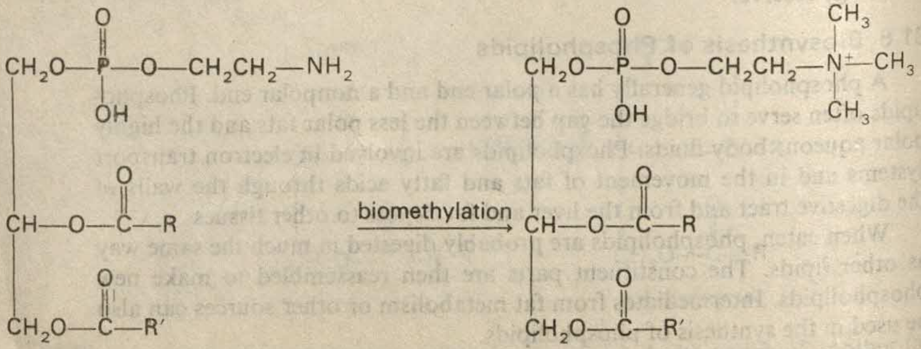
Then the ethanolamine phosphate is coupled to a cytidine nucleotide. The cytidine nucleotide acts as a carrier or activator; it picks up one molecule and ultimately transfers it to another molecule. In this case, cytidine triphosphate (CTP) reacts with the ethanolamine unit.

$$CTP + phosphoethanolamine \longrightarrow CDP—ethanolamine + P_2O_7^{4-}$$

CDP then transfers the ethanolamine unit with one phosphate unit to a diglyceride molecule.

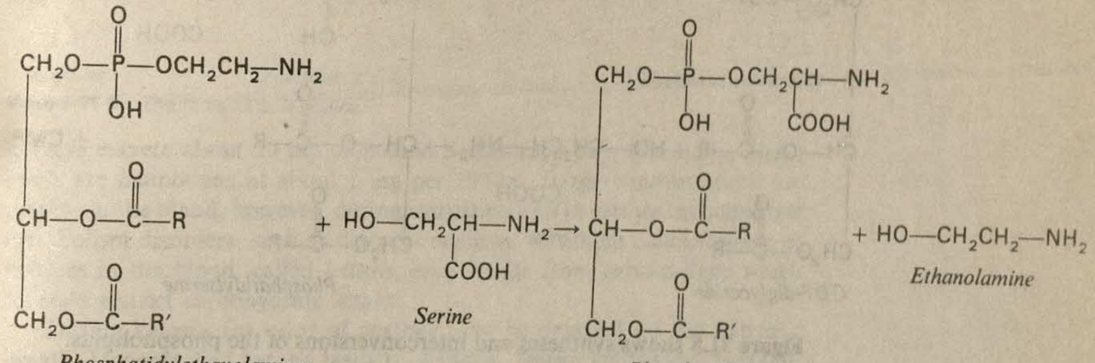
$$CDP—ethanolamine + diglyceride \longrightarrow phosphatidylethanolamine + CMP$$

The phosphatidylethanolamine can be biomethylated to form phosphatidylcholine, a lecithin (chapter 23).



Phosphatidylethanolamine *Phosphatidylcholine*

Or the phosphatidylethanolamine can exchange its ethanolamine unit, under the influence of an enzyme, for a serine unit.



Phosphatidylethanolamine

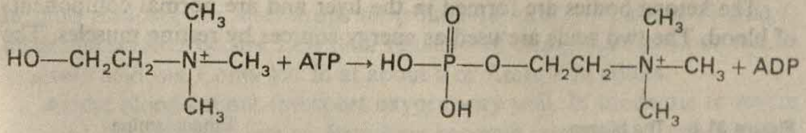
Serine

Phosphatidylserine

Ethanolamine

The product, phosphatidylserine, is another cephalin.

Phosphatidylethanolamine does not always serve as an intermediate in the preparation of other phospholipids. The cytidine nucleotide carrier can pick up a choline unit (obtained in the diet) rather than an ethanolamine unit and transfer it directly to the diglyceride molecule.



$$HO-CH_2CH_2-\overset{CH_3}{\underset{CH_3}{N^{\pm}}}-CH_3 + ATP \rightarrow HO-\overset{O}{\underset{OH}{\overset{\|}{P}}}-O-CH_2CH_2-\overset{CH_3}{\underset{CH_3}{N^{\pm}}}-CH_3 + ADP$$

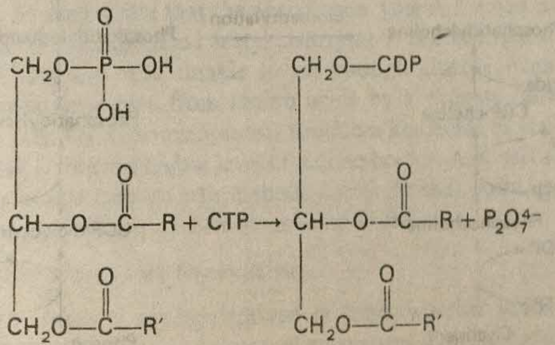
Choline

Phosphocholine

Phosphocholine + CTP ⟶ CDP—choline + $P_2O_7^{4-}$

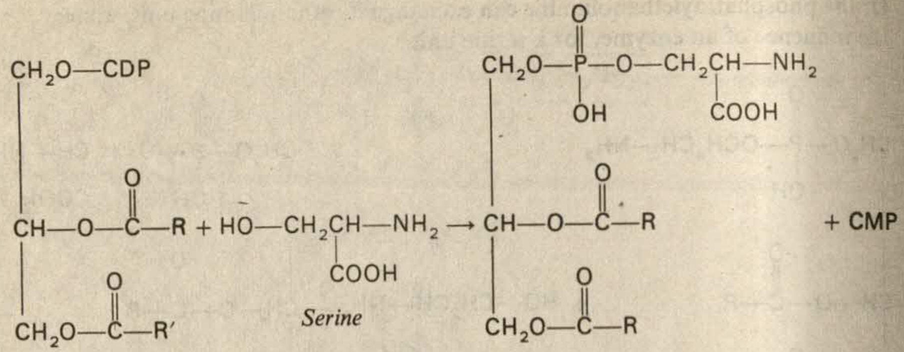
CDP—choline + diglyceride ⟶ phosphatidylcholine + CMP

Finally, bacteria reverse the whole process. In bacteria the phosphorylated diglyceride (phosphatidic acid) is picked up by the cytidine nucleotide and transferred to the alcohol unit (serine, for example).



Phosphatidic acid

CDP-diglyceride



CDP-diglyceride

Serine

Phosphatidylserine

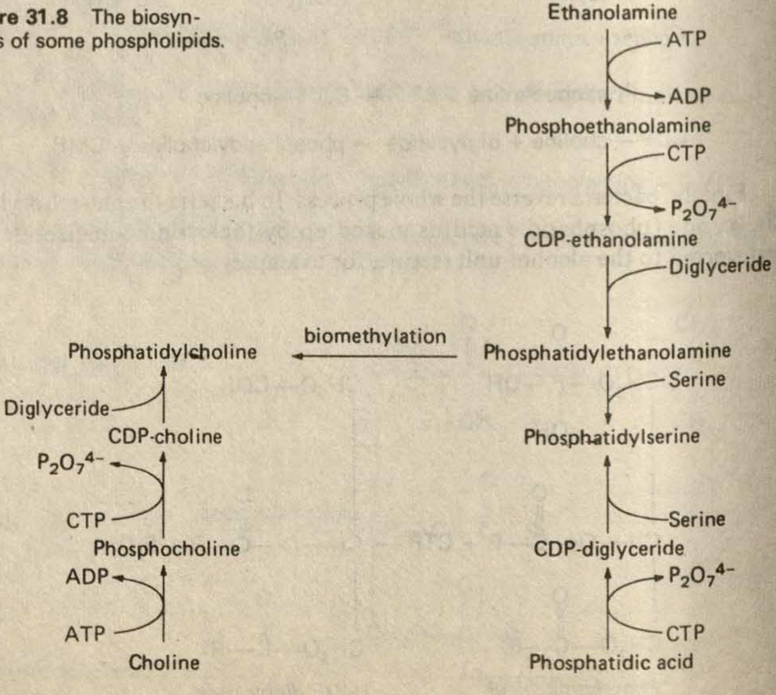
Figure 31.8 shows syntheses and interconversions of the phospholipids.

31.7 Agent XXX and the Ketone Bodies

Two related compounds, acetoacetic acid and β-hydroxybutyric acid, are intermediates in the fatty acid spiral (section 31.3). A third compound, acetone, is formed by the decarboxylation of acetoacetic acid. Collectively, these three compounds are called the *ketone bodies* (even though one is *not* a ketone). The relationship among the three is shown in **figure 31.9.**

The ketone bodies are formed in the liver and are normal components of blood. The two acids are used as energy sources by resting muscles. The

Figure 31.8 The biosynthesis of some phospholipids.



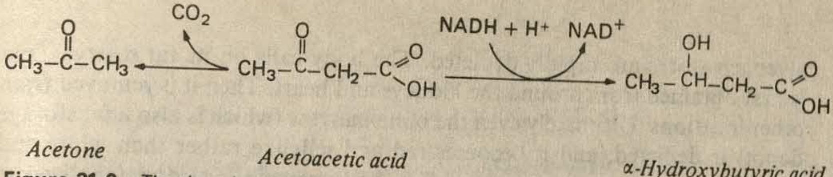


Figure 31.9 The three ketone bodies.

kidneys excrete about 20 mg of ketone bodies each day. Normally, blood levels are maintained at about 1 mg per 100 ml. Large concentrations are present in the blood, however, during starvation and in certain carbohydrate metabolism disorders, such as diabetes mellitus. This high concentration of ketones in the blood, called *ketosis,* also results from certain diets which severely restrict carbohydrate intake.

During ketosis, the odor of acetone may be detected on the patient's breath. Uncontrolled ketosis leads to acidosis. Severe ketosis can be fatal.

31.8 Acidosis: Uncontrolled Diabetes

Two of the ketone bodies are carboxylic acids. Continued production of these acids in amounts larger than the kidneys can excrete leads to *acidosis.* More acids are produced than the blood buffers can handle. The pH of the blood drops. Bicarbonate ions are used up as the buffers act to maintain constant pH. Normal bicarbonate concentration ranges from 24 to 31 meq/ℓ. In mild acidosis, the level drops to around 18 meq/ℓ. At about 13 meq/ℓ, moderate acidosis occurs. Less than 10 meq/ℓ of bicarbonate in blood results in severe acidosis. Coma sets in at about 6 or 7 meq/ℓ in adults.

Acidic blood cannot transport oxygen very well. In moderate to severe acidosis, "air hunger" sets in. Breathing becomes labored and very painful. The body also loses fluids as the kidneys eliminate large quantities of water trying to get rid of the acids. The patient becomes dehydrated. The short oxygen supply and dehydration lead to depression. Even mild acidosis leads to lethargy, loss of appetite, and a generally run-down feeling.

Untreated diabetes mellitus leads to ketosis and subsequent acidosis. Insulin is needed to transport glucose across cell membranes. In the diabetic, this transport process is interrupted. Very little glucose is burned to produce energy, and most body tissues switch over to fat metabolism. Adipose tissue releases fatty acids into the bloodstream. These are metabolized, primarily in the liver, at such a rate that the acetyl coenzyme A formed overloads the Krebs cycle. The accumulated acetyl coenzyme A is converted to the ketone bodies. Further, the cells, unable to get enough glucose from the blood, begin to make their own from amino acids by a process called *gluconeogenesis* (chapter 32) Gluconeogenesis produces ketoacids as well as glucose, and the result is an even higher level of ketone bodies. Acidosis soon follows. Untreated patients may go into diabetic coma. At that point, prompt treatment is necessary if the patient's life is to be saved.

31.9 The Chemistry of Starvation

When the body is totally deprived of food, whether voluntarily or involuntarily, the condition is known as starvation. During total fasting, the glycogen stores are rapidly depleted. The body calls on its fat reserves. Fat is first obtained from around the kidneys and heart. Then it is removed from other locations. Ultimately even the bone marrow (which is also a fat storage depot) is depleted, and it becomes red and jellylike rather than white and firm. In the early stages of a total fast, body protein is also metabolized at a relatively rapid rate. After several weeks, the rate of protein breakdown slows considerably as the brain adjusts to using fatty acid metabolites for its energy source. When no more fat reserves remain, the body must again draw heavily on structural protein for its energy requirements. The emaciated appearance of a starving individual is due to depleted muscle protein.

Figure 31.10 Starvation is a fact of life for many people in underdeveloped countries. (Courtesy of the U.S. Agency for International Development, Washington, D.C.)

In the early stages of starvation, people may riot, but they soon become docile and placid as ketosis appears and acidosis rapidly follows. Oxygen deprivation leads to depression and lethargy. Even the ability to think clearly and make decisions is impaired. A starving person often dies quietly.

Starvation is seldom the sole cause of death. Weakened by starvation, a person succumbs to disease. Even "minor" diseases such as chicken pox and measles become life-threatening disorders. Barring disease, starvation alone will lead to death from circulatory failure as the heart muscle becomes too weak to pump blood.

31.10 Too Much of a Good Thing

One of the anomalies of our time is that, while much of the world suffers from hunger and malnutrition, the major dietary problem in industrialized or developed nations is *obesity*. We eat too much, and our bodies store the excess fat in our fat depots. In rare cases, obesity is due to glandular malfunctions. The overwhelming majority of obese people are that way, though, because they eat more food than their bodies use as fuel. Adults need food primarily for the energy it can supply. Amounts eaten in excess of immediate energy requirements are stored as fat.

Extra weight puts an extra load on the heart. Not only must the body move a greater bulk around, but the heart must supply blood to more tissue.

There are many diets available for reducing one's weight. And there are many best-selling books enriching authors who recognize the public's interest in weight reduction. All successful reducing diets, though—regardless of the gimmick—have one thing in common: food intake is reduced to less than the amount burned for the production of energy. If you eat more food than you need, you gain weight. If you eat less food than you need, you lose weight. And that's the way it is.

Obesity is a major factor in diseases of the heart and circulatory system. Too much food, whether taken in as fat, carbohydrate, or protein, leads to the storage of fat. And it is this fat which shortens our life spans, killing us slowly through increased stress on the heart and arteries.

31.11 Cholesterol and Some Other Steroids

Steroids are lipids, but they are usually distinguished from the fats or phospholipids because of their unique structure (chapter 23). Fats, for example, are esters, and they can be readily hydrolyzed. Steroids are nonsaponifiable lipids; they cannot be hydrolyzed.

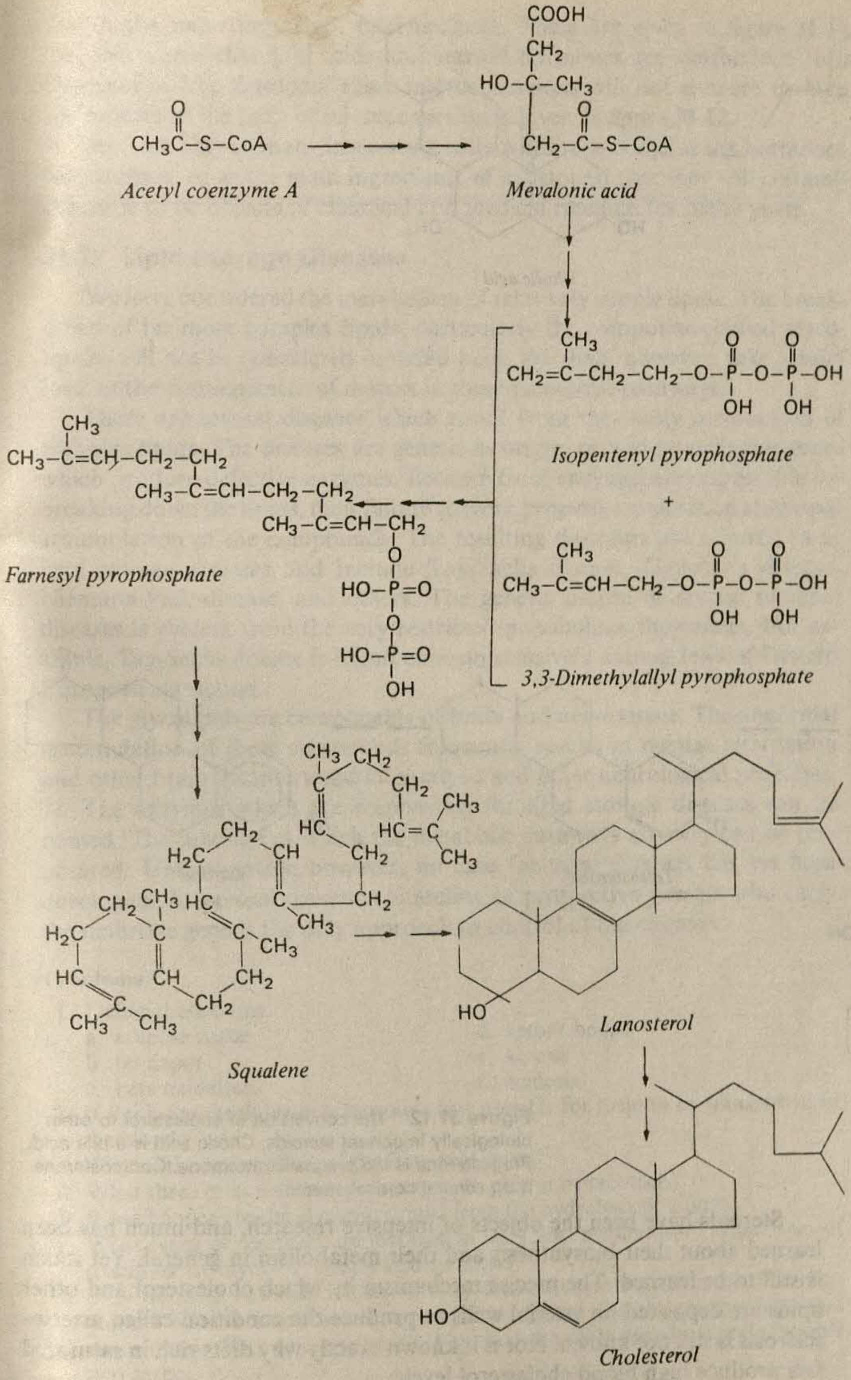


Figure 31.11 The biosynthesis of cholesterol. The basic steroid skeleton can be constructed from acetyl coenzyme A.

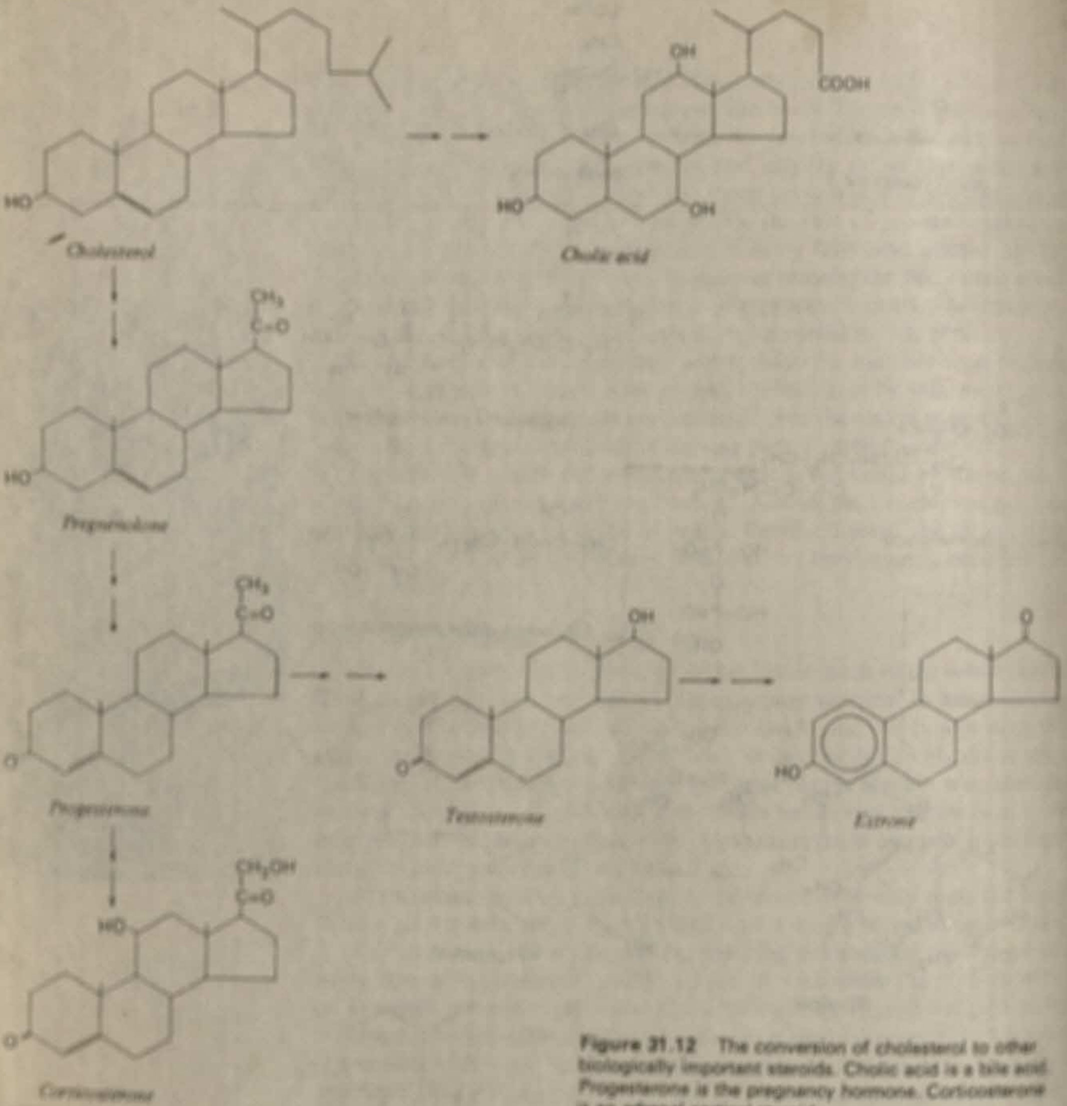


Figure 31.12 The conversion of cholesterol to other biologically important steroids. Cholic acid is a bile acid. Progesterone is the pregnancy hormone. Corticosterone is an adrenal cortical steroid.

Steroids have been the objects of intensive research, and much has been learned about their biosynthesis and their metabolism in general. Yet much is still to be learned. The precise mechanism by which cholesterol and other lipids are deposited on arterial walls to produce the condition called arteriosclerosis is still not known. Nor is it known exactly why diets rich in saturated fats produce high blood cholesterol levels.

What is known? The details of cholesterol biosynthesis have been worked out. The synthetic pathway is so long, however, that we shall simply list a few of the more important intermediates. These are given in **figure 31.11.** We also know that bile acids and steroid hormones are synthesized from cholesterol. The details of these interconversions will not concern us here. An outline of the path of interconversion is given in **figure 31.12.**

Steroids play so many interesting roles within the body (as sex hormones, for example, or as the main ingredients of gallstones) that they will certainly continue to be objects of chemical and medical research for many years.

31.12 Lipid Storage Diseases

We have considered the metabolism of relatively simple lipids. The breakdown of far more complex lipids, particularly the compounds called glycolipids, will not be considered in detail here. We shall, however, take a brief look at the consequences of defects in these metabolic pathways.

There are several diseases which result from the faulty metabolism of complex lipids. The diseases are genetic in origin, caused by defective genes which produce defective enzymes. Because these enzymes are responsible for breaking down the lipids, their failure to work properly results in an abnormal accumulation of the compounds. The resulting disorders are referred to as *lipid storage diseases* and include Tay-Sachs disease, Gaucher's disease, Niemann-Pick disease, and others. The genetic nature of several of these diseases is evident from the very restricted populations they affect. For example, Tay-Sachs disease is found almost exclusively among Jews of Eastern European extraction.

The glycolipids are components of brain and nerve tissue. The abnormal accumulation of these compounds frequently results in mental retardation and other brain disorders and in paralysis and other neurological problems.

The enzymes which are responsible for lipid storage diseases can be named. The juncture at which the metabolic pathways go awry can be pinpointed. Unfortunately, however, no cure for these diseases has yet been developed. At present, genetic counseling of prospective parents who carry the defective gene is the only approach to control of the diseases.

Problems

1. Define these terms.
   a. adipose tissue
   b. fat depot
   c. beta oxidation
   d. ketone bodies
   e. ketosis
   f. acidosis
2. If lipids are insoluble in water, how is it possible for them to be transported in the blood?
3. What is the end product of the fatty acid spiral?
4. What three roles does acetyl coenzyme A play in metabolism?
5. What happens to the glycerol formed from the hydrolysis of a fat?
6. What types of reactions are involved in fatty acid metabolism? What types of reactions are involved in fatty acid synthesis?
7. Why do most naturally occurring fatty acids have an even number of carbon atoms? What three-carbon compound is condensed with the growing fatty acid chain during fatty acid synthesis? Why does the chain length increase by units of two carbon atoms?
8. What are three functions of fats (adipose tissue) in the body?
9. What is the principal cause of obesity?
10. What is the role of cytidine triphosphate in phospholipid synthesis?

11. What common steroid serves as a starting material for steroid hormone synthesis in the body?
12. Compare and contrast glycogen and adipose tissue as reserve energy sources.
13. During a fast, what energy reserves are used first? What energy reserves supply the major part of the body's needs? What is the final source of energy called on by the body?
14. Why does acidosis result from ketosis?
15. Why does starvation result in acidosis?
16. How does lack of insulin lead to acidosis?
17. Use equations to show how acetone and β-hydroxybutyric acid are formed from acetoacetic acid.
18. How many turns around the fatty acid spiral are necessary for palmitic acid to be completely converted to acetyl coenzyme A? How many molecules of $FADH_2$ would be formed? How many molecules of NADH would be formed? How many ATP molecules are formed in the complete oxidation of palmitic acid? (Refer to section 31.3).
19. What is the origin of the lipid storage diseases? What type of tissue is particularly susceptible to the effects of these diseases?

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chapter 32

Protein Metabolism

Consider green plants. If proper amounts of nutrients—nitrates, phosphates, sulfur compounds, and so on—are available, green plants can make all the amino acids they need. From these the plants put together all their necessary protein. We poor animals are not quite so versatile. We too can put together all the proteins we require, but only if we eat properly. There are eight amino acids which we need for protein synthesis but cannot make. These *essential amino acids* (chapter 24) must be included in our diet. Perhaps if we turn green with envy . . . .

Proteins are the very stuff of our existence. They make up structural tissues such as muscles and tendons. The all-important enzymes are proteins. Some hormones are proteins. Our bodies must be able to make all of the myriad proteins that we require from those that we eat. The process of building proteins for growth, replacement, and repair is called *anabolism.* Proteins in excess of those needed for anabolism can be torn down and used for energy. That process is called *catabolism.*

Proteins—we build them, we destroy them. As long as all is in a beautiful dynamic balance, we are healthy. That's life.

32.1 Need Temporary Tissue Help? Call On the Amino Acid Pool

Carbohydrates can be stored in the liver and muscles as glycogen. Fats can be placed on reserve in the fat depots. For proteins, however, there are no comparable storage facilities. Proteins are digested in the small intestine and the resulting amino acids are absorbed directly into the bloodstream. Here they join a circulating pool of amino acids.

Members of the amino acid pool are there only on temporary assignment. New members are constantly added to the pool, and old ones are regularly withdrawn. The body can supply the pool by synthesizing amino acids from scratch or by breaking down tissue protein to obtain the constituent amino acids. It drains the pool to obtain raw materials for new protein synthesis or for the synthesis of other nitrogen-containing compounds such as heme. It can also use the amino acids as a source of energy. The nitrogen stored in the pool cannot be recycled within the body endlessly. Each day some of the amino acids are catabolized and the nitrogen is eliminated from the body as urea. This represents a net drain of material from the pool. It is to compensate for this drain that we require proteins in our diet.

Ingested proteins satisfy two needs. First, they provide nitrogen to replace that which has been eliminated from the body. Although the nitrogen comes in as part of specific amino acid residues, the body has a considerable capacity for shifting that nitrogen around (section 32.4). In this respect, then, the ingested protein acts simply as a source of nitrogen.

In addition to serving as a general source of nitrogen, dietary protein must also supply some specific amino acids. These are the essential amino acids. The body cannot put together the carbon skeletons of these compounds. Yet amino acids with these skeletons are required for protein synthesis, among other things. By eating complete proteins (those which contain essential amino acid residues), we see to it that the amino acid pool is regularly resupplied with the amino acids we cannot synthesize ourselves.

The relationship between the amino acid pool and other aspects of protein metabolism is shown in **figure 32.1**.

32.2 Turnover: The Ins and Outs of Body Proteins

Just as amino acids are only temporary participants in the amino acid pool, so, too, are specific protein molecules only temporary residents in the body. Our bodies continually take in proteins and break them down into

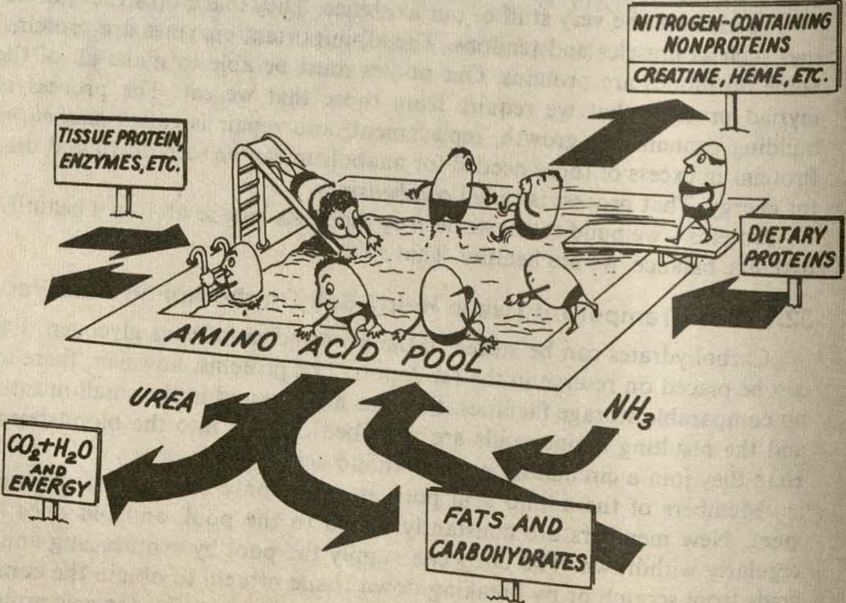


Figure 32.1 The amino acid pool and protein metabolism.

their constituent amino acids. The liver and other body tissues take these amino acids and incorporate them into new proteins. Structural proteins, enzymes, and proteinlike hormones are continually being degraded and rebuilt. Our proteins are in a state of dynamic equilibrium as "old" ones are hydrolyzed and "new" ones are synthesized.

The amount of protein synthesized or degraded per unit time gives the *turnover rate*. The rate is different for proteins in different kinds of body tissue. *Turnover times* represent the average residence time for a protein molecule in the tissues. Turnover times are usually expressed as half-lives. A half-life is the time interval in which one-half of the protein molecules in a given tissue have been replaced. Liver proteins and those in the blood plasma have rapid turnovers, with half-lives of from 2 to 10 days. Muscle proteins have a more stable employment, with half-lives of about 6 months. Some collagen molecules may hang around for 3 years.

Protein synthesis is carried on continuously in the body. Its control by the genetic code and an outline of its mechanism were given in chapter 25. Protein synthesis is limited by the availability of each of the eight essential amino acids. For example, if a given protein requires 4 units of phenylalanine per molecule and 40 are available, only 10 protein molecules can be made even though there may be enough of all the other amino acids to make a million protein molecules. Within these limits, proteins are synthesized as needed by our bodies.

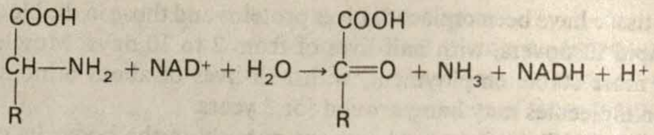
The state of the protein equilibrium within the body is usually evaluated by measurement of the amount of nitrogen being taken into and excreted from the body. As long as the amount of nitrogen taken in is equal to the amount of nitrogen excreted, a person is said to be in *nitrogen balance*. During growth or substantial repair of body tissues, more nitrogen is taken in than is excreted. Growing children and adults who are recovering from starvation or wasting illness are in such a state of *positive nitrogen balance*. Starvation and debilitating disease may result in a *negative nitrogen balance;* less nitrogen is ingested than is excreted. Diets lacking sufficient quantities of one or more of the essential amino acids also result in the excretion of more nitrogen than is taken in.

32.3 Amino Acid Metabolism: Remove the Nitrogen and All Things Are Possible

If amino acids are taken from the pool for something other than protein synthesis, then the elimination of the amino group is frequently the first step in the metabolic pathway. There is a set of reversible reactions which serves as a link between amino acid catabolism and synthesis. As they proceed in one direction, these reactions result in the removal of the amino group of an amino acid. The reverse reactions provide a means for attachment of an amino group to form a new amino acid. There are two reactions in the set. They are called, respectively, *oxidative deamination* and *transamination*. We shall consider first the catabolism of amino acids by way of these reactions.

Some of the proteins we eat are used for the production of energy. Protein eaten in excess of that needed for energy or for growth, replacement, and repair of tissue is converted to glycogen or to fat for storage. First the proteins are hydrolyzed to amino acids. These enter the amino acid pool. If they are to be burned for energy or processed for storage as fat or glycogen, the amino acids must be converted to intermediates of the Krebs tricarboxylic acid cycle or to pyruvic acid or acetyl coenzyme A. In all cases, the amino acid must first be stripped of its amino group.

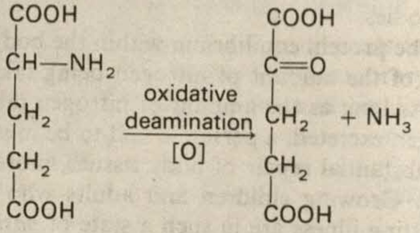
In oxidative deamination the amino acid is converted to a keto acid and the amino group is released as ammonia. (Actually it is an ammonium ion which is formed, but we shall adopt the convention of writing this product, as well as the amino acids, in their un-ionized forms.)



$$\mathrm{R{-}CH(NH_2){-}COOH} + \mathrm{NAD^+} + \mathrm{H_2O} \rightarrow \mathrm{R{-}C({=}O){-}COOH} + \mathrm{NH_3} + \mathrm{NADH} + \mathrm{H^+}$$

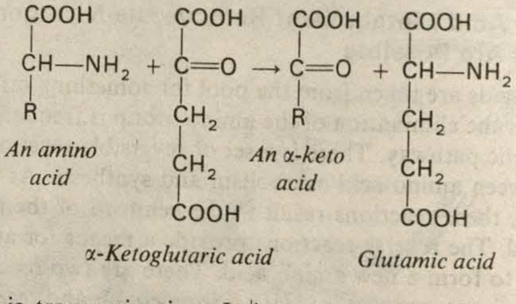
The ammonia can be converted to urea (section 32.5) and excreted. The NADH is reoxidized in the electron transport chain (chapter 30).

Biochemists have isolated many enzymes which will catalyze the oxidative deamination of a variety of amino acids. However, the only compound for which this is a significant metabolic route is glutamic acid.



Glutamic acid *α-Ketoglutaric acid*

How are other amino acids deaminated? Most of them simply transfer their amino group to α-ketoglutaric acid.



α-Ketoglutaric acid *Glutamic acid*

This reaction is transamination. It is catalyzed by enzymes called transaminases. The reaction requires the coenzyme pyridoxal phosphate. It does not necessarily require α-ketoglutaric acid as the amino group acceptor. Many keto acids can act as nitrogen acceptors in transaminations. The most frequently encountered transaminations, however, incorporate the α-keto-

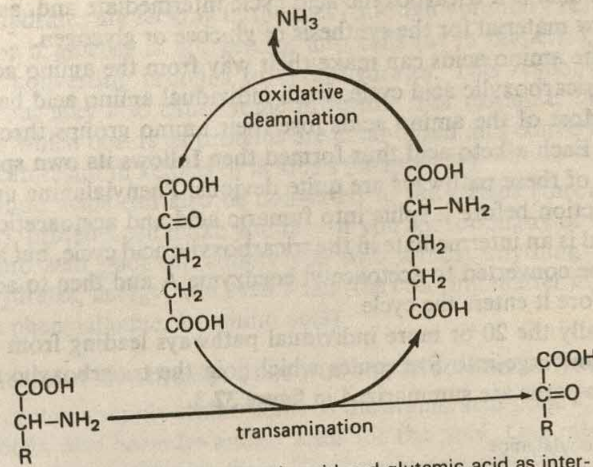
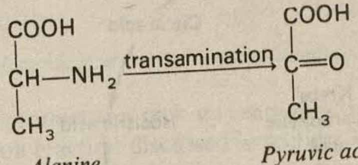


Figure 32.2 α-Ketoglutaric acid and glutamic acid as intermediates in the deamination of amino acids.

glutaric/glutamic acid combination. The other product of the reaction is an α-keto acid corresponding to the original amino acid. Transamination simply involves an exchange of functional groups.

The glutamic acid formed in this reaction can undergo oxidative deamination. Through this combination of transamination–oxidative deamination an amino acid's amino group is converted to ammonia. **Figure 32.2** shows that glutamic acid is merely an intermediate in this process. The nitrogen released by glutamic acid as ammonia can originate in any amino acid.

If the amino acid which transfers its amino group to α-ketoglutaric acid is alanine, the keto acid product of the transamination is pyruvic acid.

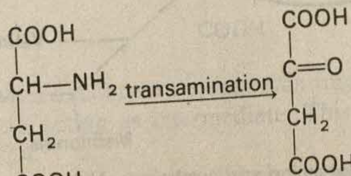


$$\mathrm{HOOC{-}CH(NH_2){-}CH_3} \xrightarrow{\text{transamination}} \mathrm{HOOC{-}C(=O){-}CH_3}$$

Alanine *Pyruvic acid*

Pyruvic acid can be converted to acetyl coenzyme A. The acetyl coenzyme A can be degraded through the tricarboxylic acid cycle to produce energy or can be used for fatty acid synthesis. Pyruvic acid itself represents a starting material for glycogen synthesis.

Aspartic acid is converted to oxaloacetic acid through transamination.



$$\mathrm{HOOC{-}CH(NH_2){-}CH_2{-}COOH} \xrightarrow{\text{transamination}} \mathrm{HOOC{-}C(=O){-}CH_2{-}COOH}$$

Aspartic acid *Oxaloacetic acid*

Oxaloacetic acid is a tricarboxylic acid cycle intermediate and, as such, represents a raw material for the synthesis of glucose or glycogen.

All of the amino acids can make their way from the amino acid pool to the Krebs tricarboxylic acid cycle. Each individual amino acid has a unique pathway. Most of the amino acids lose their amino groups through transamination. Each α-keto acid thus formed then follows its own special pathway. Some of these pathways are quite devious. Phenylalanine undergoes a six-step reaction before it splits into fumaric acid and acetoacetic acid. The fumaric acid is an intermediate in the tricarboxylic acid cycle, but acetoacetic acid must be converted to acetoacetyl coenzyme A and then to acetyl coenzyme A before it enters the cycle.

Eventually the 20 or more individual pathways leading from the amino acid pool converge into five routes which join the tricarboxylic acid cycle. The various paths are summarized in **figure 32.3**.

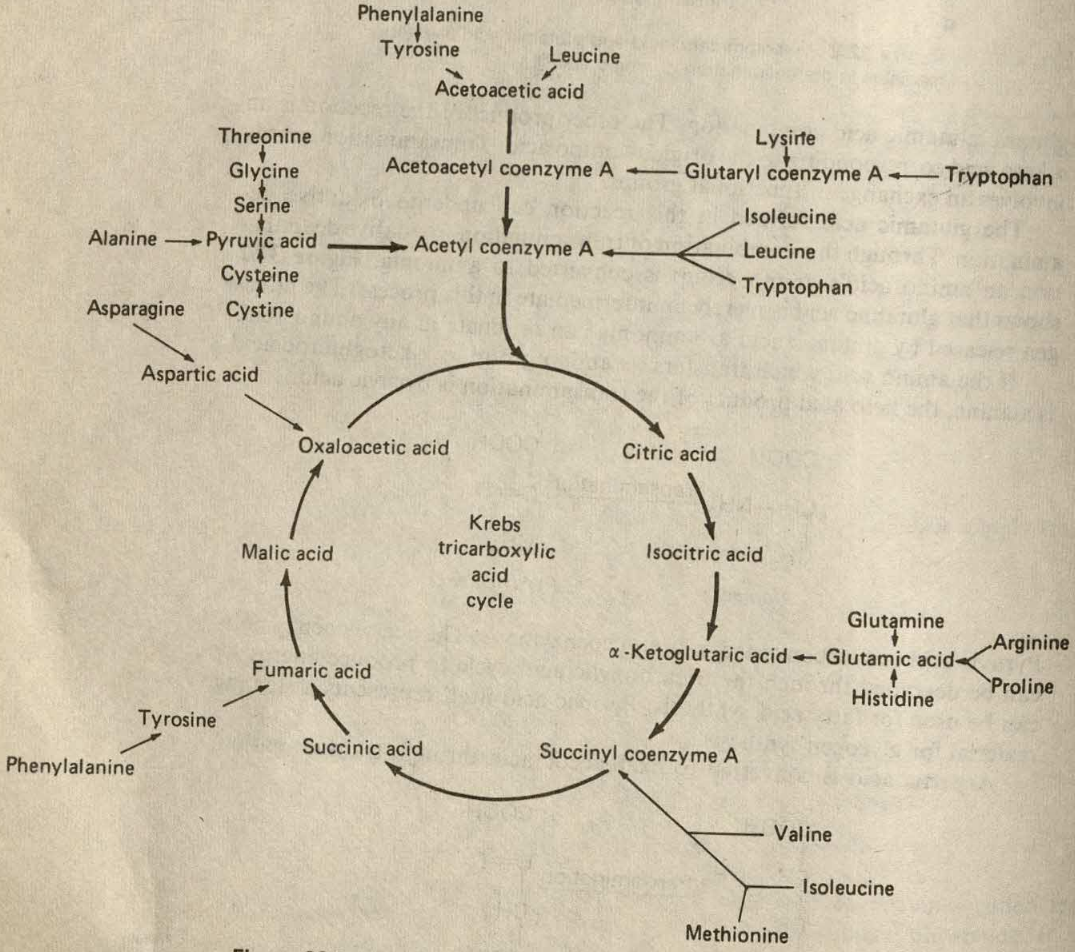


Figure 32.3 Pathways of amino acid catabolism. All lead eventually to the Krebs tricarboxylic acid cycle.

If carbohydrates are lacking in the diet (through voluntary restriction or starvation) or if glucose is not getting into cells (as in diabetes), the body responds by converting proteins to carbohydrates. This response satisfies some needs but may also cause some problems. For example, the buildup of keto acids which occurs as proteins are catabolized and converted to carbohydrates can result in ketosis or acidosis (chapter 31).

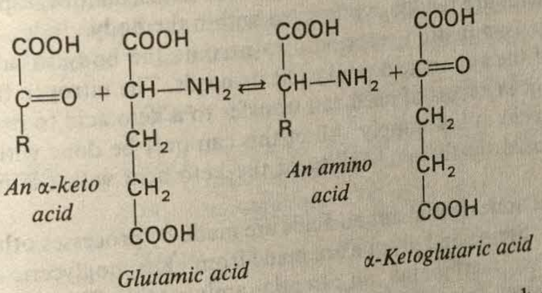
Since amino acids can also be converted to fatty acids (through acetyl coenzyme A), proteins can make you fat—if you eat too many of them.

The amino acid pool can supply you with almost anything—proteins, fats, carbohydrates, energy, and even a tan (the coloring matter in your skin starts out as phenylalanine, an amino acid).

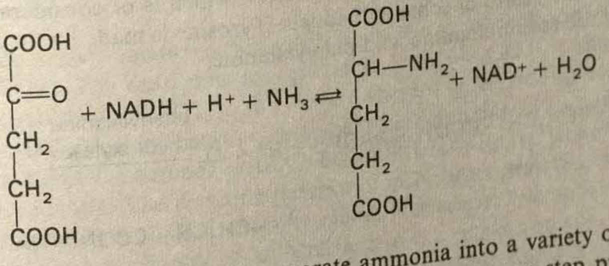
32.4 Amino Acid Synthesis: Just Put the Machine in Reverse

Dietary proteins supply amino acids to the amino acid pool. Catabolism of tissue protein also provides amino acids for the pool. One other way to get amino acids is to synthesize them. The liver is particularly good at that.

Transamination provides a route from available α-keto acids to amino acids. In section 32.3 we considered this reaction as a way of removing amino groups from a variety of amino acids. Now we will concentrate on the reverse reaction, in which glutamic acid usually serves as a source of nitrogen for the synthesis of other amino acids.



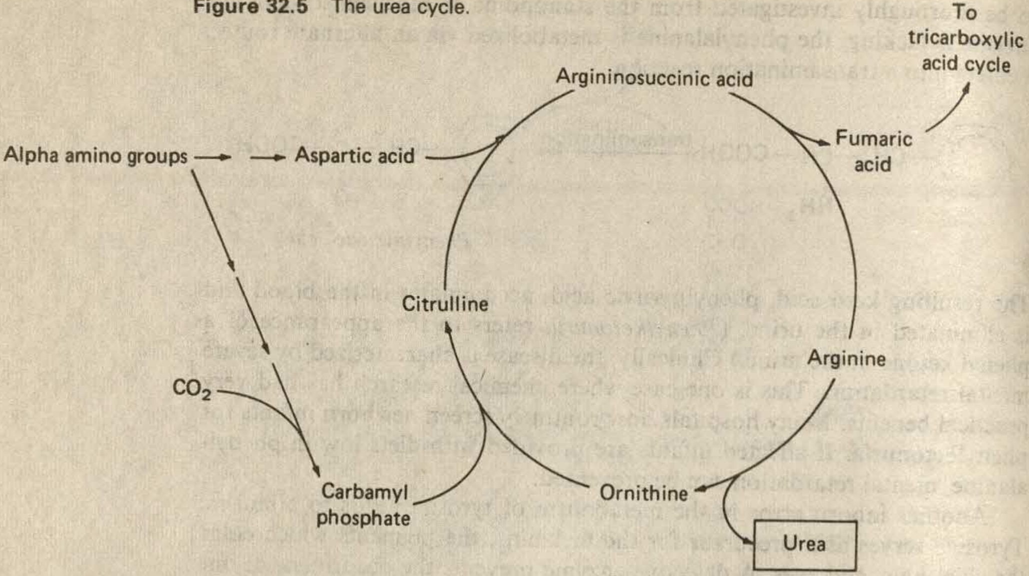
The α-ketoglutaric acid product can pick up ammonia through a reversal of the oxidative deamination reaction discussed in section 32.3.



The two reactions combined incorporate ammonia into a variety of amino acids, with glutamic acid acting as intermediate. This two-step process is summarized in **figure 32.4.**

The body can't synthesize the essential amino acids, because it cannot make the corresponding α-keto acids. In contrast, keto acids such as pyruvic

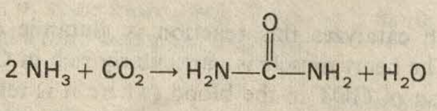
Figure 32.5 The urea cycle.



The synthesis of aspartic acid through this transamination reaction is very important to animals who excrete nitrogen in the form of urea. Aspartic acid is needed for the synthesis of urea. We shall consider this synthesis in detail in the next section.

32.5 Flowing Around the Urea Cycle

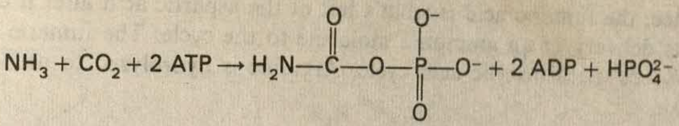
The Wright brothers invented airplanes. Henry Ford made automobiles. Hans Krebs invented cycles. We have encountered his citric acid cycle of carbohydrate metabolism several times. Krebs also worked out the *urea cycle*, or, as it is sometimes called, the *ornithine cycle*. The urea cycle describes the reactions by which the nitrogen released in amino acid metabolism is converted to the compound urea. These reactions occur in the liver. The *net* reaction of the cycle involves the synthesis of urea from ammonia and carbon dioxide.



$$2\ NH_3 + CO_2 \longrightarrow H_2N\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}NH_2 + H_2O$$

The stepwise process of the urea cycle is summarized in **figure 32.5**. The ammonia molecules shown in the net reaction enter the cycle in disguise, using two routes. One route brings the ammonia in as the amino group of an amino acid. The second route requires the input of a carbon dioxide molecule as well as an ammonia molecule. The ammonia is provided through the oxidative deamination of amino acids (section 32.3). Let's focus on the second route.

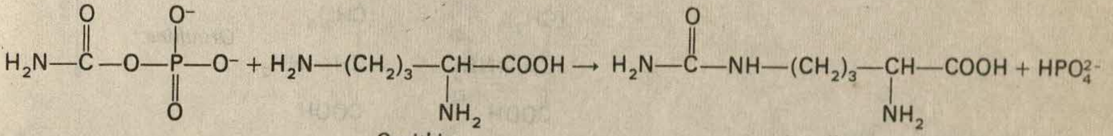
Carbon dioxide combines with ammonia in the presence of ATP to form carbamyl phosphate.



$$NH_3 + CO_2 + 2\,ATP \rightarrow H_2N-\overset{\overset{O}{\|}}{C}-O-\underset{\underset{O}{\|}}{\overset{\overset{O^-}{|}}{P}}-O^- + 2\,ADP + HPO_4^{2-}$$

Carbamyl phosphate

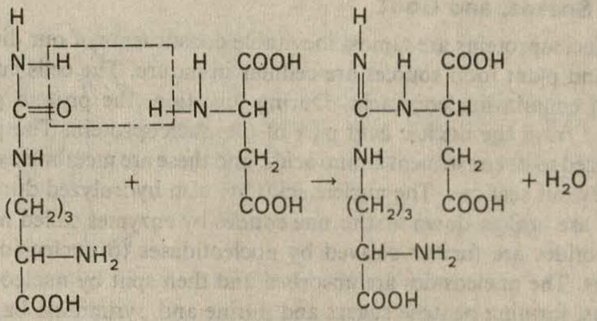
Carbamyl phosphate is a high-energy compound. It reacts with a basic amino acid named ornithine to form citrulline.



$$H_2N-\overset{\overset{O}{\|}}{C}-O-\underset{\underset{O}{\|}}{\overset{\overset{O^-}{|}}{P}}-O^- + H_2N-(CH_2)_3-\underset{\underset{NH_2}{|}}{CH}-COOH \rightarrow H_2N-\overset{\overset{O}{\|}}{C}-NH-(CH_2)_3-\underset{\underset{NH_2}{|}}{CH}-COOH + HPO_4^{2-}$$

Ornithine *Citrulline*

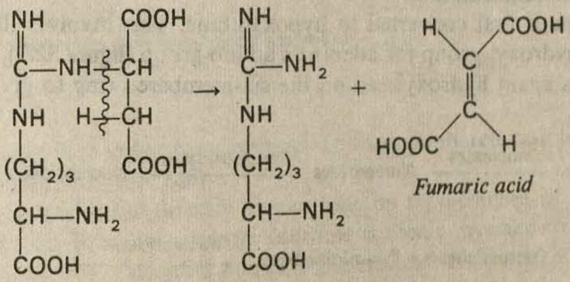
The citrulline molecule next reacts with aspartic acid. Aspartic acid represents the second entry route to the cycle. The amino groups of other alpha amino acids can be transferred to aspartic acid by a series of transamination reactions (section 32.4). The aspartic acid and the previously formed citrulline combine to produce argininosuccinic acid.



Citrulline *Argininosuccinic acid*

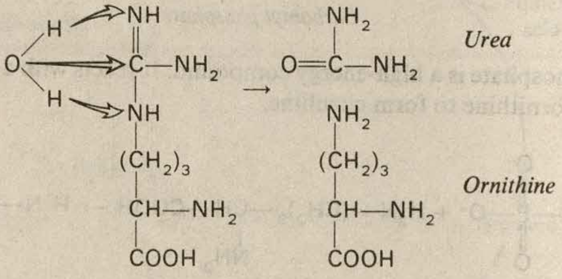
The carbon and both nitrogens required for the formation of urea have now entered the cycle.

The argininosuccinic acid splits out fumaric acid, leaving arginine.



Arginine *Fumaric acid*

In essence, the fumaric acid is what's left of the aspartic acid after it completes its delivery of an ammonia molecule to the cycle. The fumaric acid enters Krebs' tricarboxylic acid cycle. Arginine is hydrolyzed to urea and ornithine.



The urea is transported to the kidneys and excreted in urine (chapter 28). Ornithine starts another turn of the cycle by reacting with a fresh molecule of carbamyl phosphate. In human beings, over 80% of the nitrogen from protein catabolism is excreted as urea.

32.6 Nucleoprotein Metabolism: Uric Acid, Birds, Snakes, and Gout

Nucleoproteins are almost inevitable constituents of our diets. Both animal and plant food sources are cellular in nature. The cells contain nuclei; nuclei contain nucleoprotein. During digestion, the protein portion is removed from the nucleic acid part of the nucleoprotein. The protein is hydrolyzed to its constituent amino acids, and these are metabolized as described in previous sections. The nucleic acids are also hydrolyzed during digestion. They are broken down first to nucleotides by enzymes called nucleases. The nucleotides are further cleaved by nucleotidases to nucleosides and phosphates. The nucleosides are absorbed and then split by nucleosidases in the tissues, forming pentose sugars and purine and pyrimidine bases. These reactions are summarized in **figure 32.6.**

The sugars—deoxyribose and ribose—are metabolized by the usual carbohydrate pathways (chapter 30). Phosphates can be used in the formation of new phosphate compounds, or they may be excreted in the urine. The purines and pyrimidines are metabolized by different pathways. Let's look at purine metabolism first.

Adenine is first converted to hypoxanthine. This involves the substitution of a hydroxyl group for adenine's amino group (**figure 32.7**). The hypoxanthine is again hydroxylated on the six-membered ring to give xanthine.

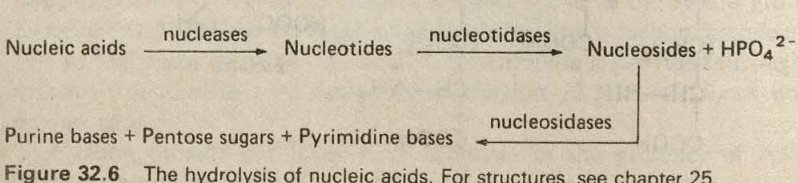

Nucleic acids
nucleases
Nucleotides
nucleotidases
Nucleosides + HPO$_4$$^{2-}$
nucleosidases
Purine bases + Pentose sugars + Pyrimidine bases

Figure 32.6 The hydrolysis of nucleic acids. For structures, see chapter 25.

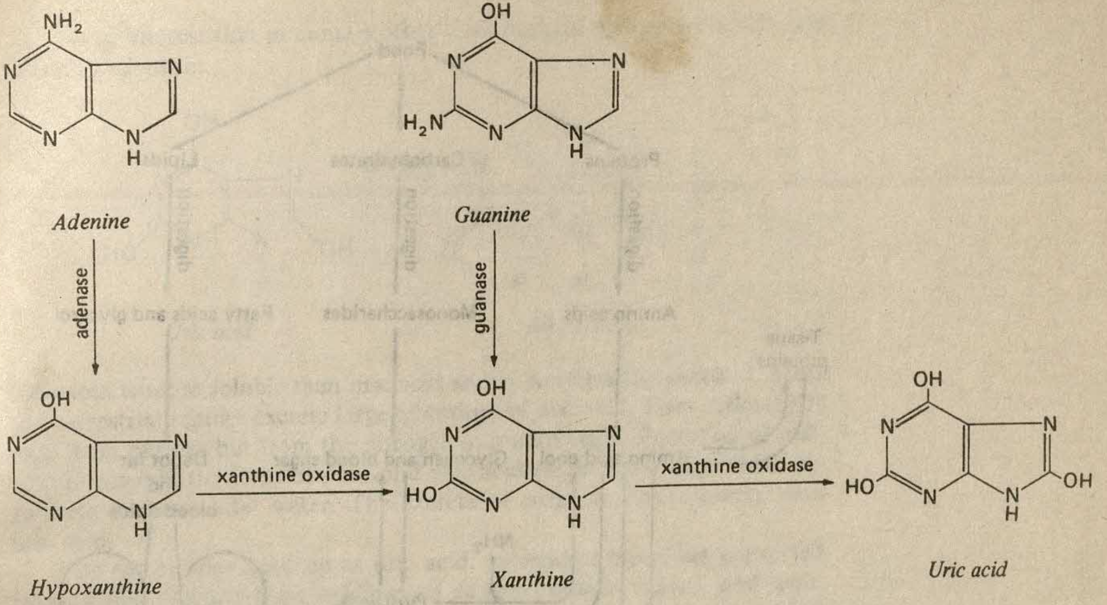


Figure 32.7 The conversion of purine bases to uric acid.

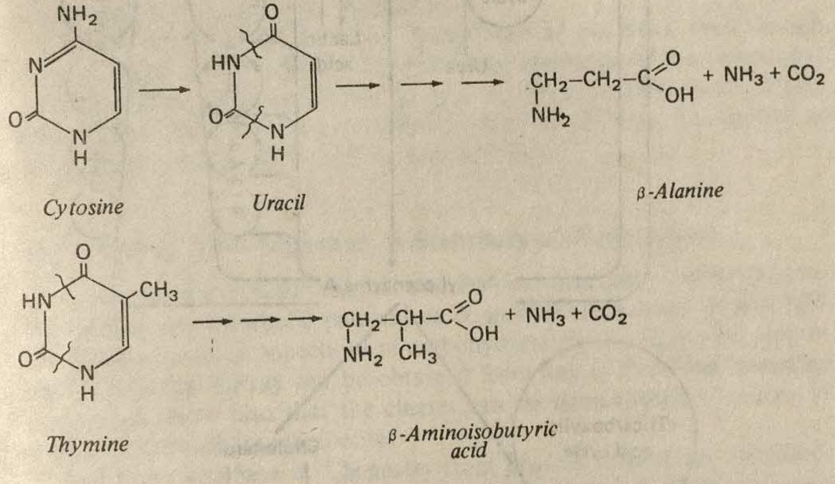


Figure 32.8 The metabolism of pyrimidine bases.

That compound is then hydroxylated on the five-membered ring to give the trihydroxy compound uric acid.

Guanine is converted directly to xanthine by replacement of its amino group by a hydroxyl group, and the xanthine is then converted to uric acid. Each of these steps is catalyzed by a specific enzyme. Uric acid is generally excreted in the urine.

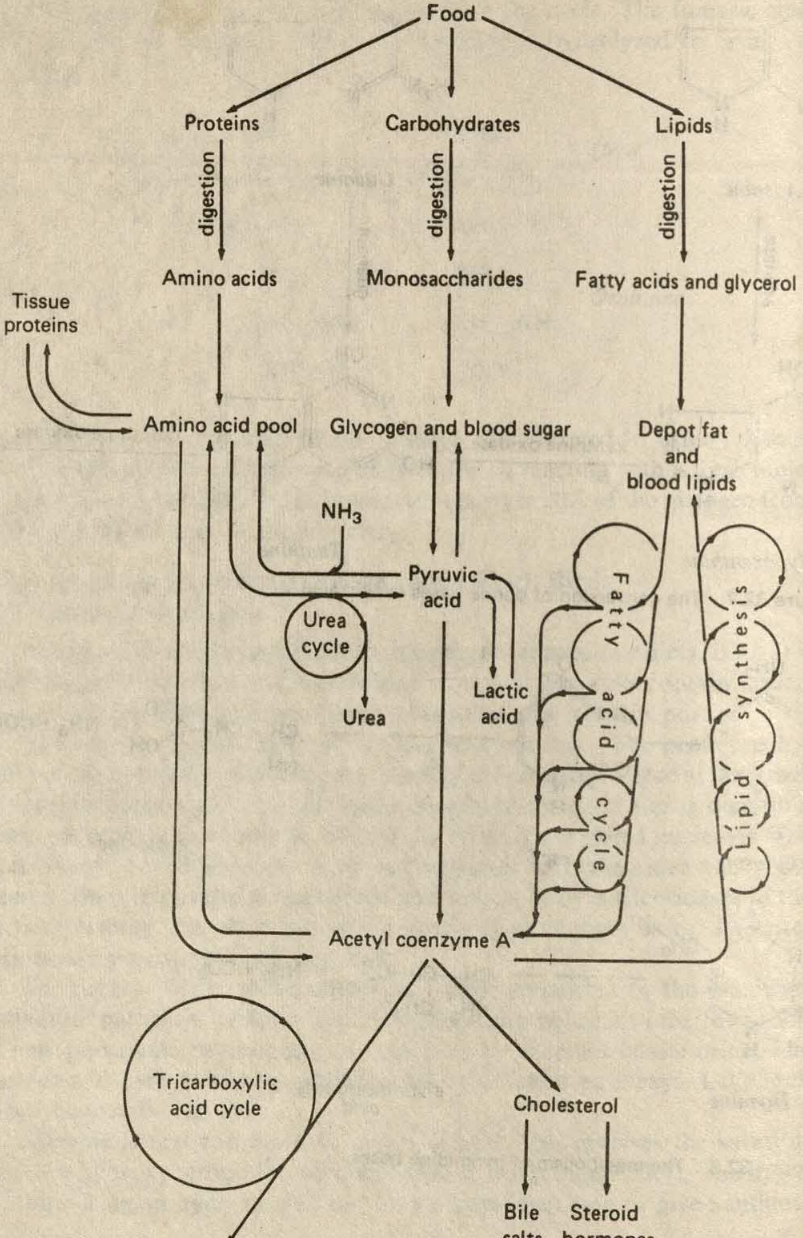
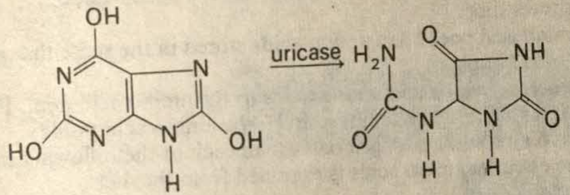


Figure 32.9 The interconnections of carbohydrate, lipid, and protein metabolism.

The painful metabolic disorder called *gout* results from the deposition of uric acid salts in cartilage. It is far more common in men than in women. Uric acid salts are also deposited in the form of kidney and bladder stones.

It is of interest that mammals other than humans and apes convert uric acid into allantoin.



Uric acid

Allantoin

Allantoin is more soluble than uric acid and is more readily excreted. Birds and terrestrial reptiles excrete large quantities of uric acid. They make it not only from purines but from the nitrogen in amino acids. Excretion of protein nitrogen in the form of semisolid uric acid suspensions helps these organisms conserve vital water. The excreta of some snakes is nearly pure uric acid.

Whereas purines wind up as uric acid, pyrimidine bases are converted to products which can be oxidized to carbon dioxide, water, and urea. Cytosine and uracil, through a series of enzyme-catalyzed reactions, wind up as β-alanine. Thymine is converted to β-aminoisobutyric acid. These conversions are summarized in **figure 32.8.**

Nucleic acids are not necessary components of our diets, even though they are nearly always present. Our bodies can synthesize all the component parts of nucleic acids, including the purine and pyrimidine bases. These bases can be made from amino acids and other metabolites. The process is quite complicated, and we will not consider it here.

32.7 Putting It All Together: A Summary of Metabolism

At several places in this chapter and the two preceding it, we have mentioned how one metabolic pathway is connected to another. **Figure 32.9** summarizes the interconnections of carbohydrate, lipid, and protein metabolism. Note that energy can be obtained from any of the three classes of compounds. Note also that the classes can be interconverted by way of common intermediate metabolites.

And there you have it. Chemistry from protons to proteins. Carbohydrate, lipid, and protein metabolism are all tied together. Indeed, in a living organism, everything is connected to everything else. Life is one huge, complicated set of chemical reactions—and, of course, a lot more. The whole of life is certainly much more than the sum of a set of chemical reactions.

We hope that we have enriched your life by helping you to learn something of the basis of chemistry and of the many ways chemistry touches your life every day. And we wish for you the proper reward for the many hours you have spent studying chemistry: the joy of success in your chosen profession.

Problems

1. Define these terms:
   a. anabolism
   b. catabolism
   c. protein turnover time
   d. positive nitrogen balance
   e. negative nitrogen balance
2. What is the amino acid pool? Are amino acids stored in the sense that glycogen and fats are stored? Explain.
3. Name three processes which add amino acids to the amino acid pool. For what purposes might amino acids be removed from the amino acid pool?
4. What happens to a person's nitrogen balance in each of the following cases?
   a. if one of the essential amino acids is excluded from the diet
   b. during fasting
   c. during recovery from a wasting illness
5. Use simplified equations to show how glutamic acid and α-ketoglutaric acid serve as intermediates in the conversion of amino acid nitrogen to ammonia. What are the names of the two reactions involved?
6. Which amino acid, upon transamination, would yield each of the following?
   a. oxaloacetic acid
   b. pyruvic acid
   c. phenylpyruvic acid
7. How does transamination serve to connect amino acid metabolism with carbohydrate and lipid metabolism?
8. Ammonia is formed in the oxidative deamination of amino acids. How is it eliminated from the human body?
9. What is the end product of purine metabolism? Of pyrimidine metabolism?
10. Must purines and pyrimidines be included in the human diet? Explain.
11. Diets high in DNA may result in the appearance of β-aminoisobutyric acid in the urine. Those high in RNA do not. Explain.
12. Name two genetic disorders connected with tyrosine metabolism. What are the characteristics of the diseases which result from these inborn errors of metabolism?
13. Explain the significance of the appearance of the enzymes SGOT and CPK in the blood.

References and Readings

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4. Meister, A., *Biochemistry of the Amino Acids,* 2 vols., 2nd ed., New York: Academic Press, 1965.
5. Stryer, Lubert, *Biochemistry,* San Francisco: W. H. Freeman, 1975. See chapter 18, "Amino Acid Degradation and the Urea Cycle."
6. Yudkin, Michael, and Offord, Robin, *Biochemistry,* Boston: Houghton Mifflin, 1975. See chapter 22 for a discussion of the metabolism of amino acids.

appendix A

The International System of Measurement

Metric measurement was discussed in some detail in chapter 1. Further discussion and additional tables are provided here.

The standard unit of length in the International System of Measurement is the *metre*. This distance was once meant to be 0.000 000 1 of the earth's quadrant, that is, of the distance from the North Pole to the equator measured along a meridian. The quadrant was difficult to measure accurately. Consequently, for many years the metre was defined as the distance between two etched lines on a metal bar (made of a platinum-iridium alloy) kept in the International Bureau of Weights and Measures at Sèvres, France. Today, the metre is defined even more precisely as being 1 650 763.73 times the wavelength of the orange-red line in the spectrum of krypton-86.

The primary unit of mass is the *kilogram* (1 kg = 1000 g). It is based on a standard platinum-iridium bar kept at the International Bureau of Weights and Measures. The *gram* is a more convenient unit for many chemical operations.

The basic SI unit of volume is the cubic metre. The unit more frequently employed in chemistry, however, is the *litre* (1 ℓ = 0.001 m^3). All other SI units of length, mass, and volume are derived from these basic units.

Table A-1
Some SI prefixes and their relationship to the basic units

Prefix	*Connotation*
Pico-	0.000 000 000 001 × (or 10^{-12} ×)
Nano-	0.000 000 001 × (or 10^{-9} ×)
Micro-	0.000 001 × (or 10^{-6} ×)
Milli-	0.001 × (or 10^{-3} ×)
Centi-	0.01 × (or 10^{-2} ×)
Deci	0.1 × (or 10^{-1} ×)
Deka-	10 × (or 10^{1} ×)
Hecto-	100 × (or 10^{2} ×)
Kilo-	1 000 × (or 10^{3} ×)
Mega-	1 000 000 × (or 10^{6} ×)
Giga-	1 000 000 000 × (or 10^{9} ×)
Tera-	1 000 000 000 000 × (or 10^{12} ×)

Table A-2
Some metric units of length

1 kilometre (km) = 1000 metres (m)
1 metre (m) = 100 centimetres (cm)
1 centimetre (cm) = 10 millimetres (mm)
1 millimetre (mm) = 1000 micrometres (μm).

Table A-3
Some metric units of mass

1 kilogram (kg) = 1000 grams (g)
1 gram (g) = 1000 milligrams (mg)
1 milligram (mg) = 1000 micrograms (μg)

Table A-4
Some metric units of volume

1 litre (ℓ) = 1000 millilitres (ml)
1 millilitre (ml) = 1000 microlitres (μl)
1 millilitre (ml) = 1 cubic centimetre (cm^3)

Table A-5
Some British-metric conversions

Length

1 mile (mi) = 1.61 kilometres (km)
1 yard (yd) = 0.914 metre (m)
1 inch (in) = 2.54 centimetres (cm)

Mass

1 pound (lb) = 454 grams (g)
1 ounce (oz) = 28.4 grams (g)
1 pound (lb) = 0.454 kilogram (kg)
1 grain (gr) = 0.0648 gram (g)
1 carat (car) = 200 milligrams (mg)

Volume

1 U.S. quart (qt) = 0.946 litre (ℓ)
1 U.S. pint (pt) = 0.473 litre (ℓ)
1 fluid ounce (fl oz) = 29.6 millilitres (ml)
1 gallon (gal) = 3.78 litres (ℓ)

Table A-6
Some conversion units for pressure'

1 millimetre of mercury (mm Hg) = 1 torr
1 atmosphere (atm) = 760 millimetres of mercury (mm Hg) = 760 torrs
1 atmosphere (atm) = 29.92 inches of mercury (in. Hg) =
1 atmosphere (atm) = 14.7 pounds per square inch (psi)

Table A-7
Some temperature equivalents*

Phenomenon	*Fahrenheit*	*Celsius*
Absolute zero	−459.69 °F	−273.16 °C
Nitrogen boils/liquifies	−320.4 °F	−195.8 °C
Carbon dioxide solidifies/sublimes	−109.3 °F	−78.5 °C
Bitter cold night, northern Minnesota	−40 °F	−40 °C
Cold night, Indiana	0 °F	−18 °C
Water freezes/ice melts	32 °F	0 °C
Pleasant room temperature	72 °F	22 °C
Body temperature	98.6 °F	37.0 °C
Very hot day	100 °F	38 °C
Water boils/steam condenses	212 °F	100 °C
Temperature for baking biscuits	450 °F	232 °C

*Keep these equations in mind.

$$°\mathrm{F} = \frac{9}{5}(°\mathrm{C}) + 32$$

$$°\mathrm{C} = (°\mathrm{F} - 32)\frac{5}{9}$$

Table A-8
Some conversion units for energy

1 calorie (cal) = 4.184 joules (J)
1 British thermal unit (Btu) = 1053 joules (J) = 252 calories (cal)
1 food "Calorie" = 1 kilocalorie (kcal) = 1000 calories (cal) = 4184 joules (J)

appendix B

Exponential Notation

Scientists often use numbers that are so large—or so small—that they boggle the mind. For example, light travels at 30 000 000 000 cm/second. There are 602 300 000 000 000 000 000 000 carbon atoms in 12 g of carbon. On the small side, the diameter of an atom is about 0.000 000 000 1 m. The diameter of an atomic nucleus about 0.000 000 000 000 001 m.

It is obviously difficult to keep track of the zeros in such quantities. Scientists find it convenient to express such numbers as *powers of ten.* **Tables B-1** and **B-2** contain partial lists of such numbers.

The speed of light is usually expressed as 3×10^{10} (i.e., $3 \times 10 \times 10 \times 10 \times 10 \times 10 \times 10 \times 10 \times 10 \times 10 \times 10$) cm/second. The mass of an atom of cesium (Cs) is expressed as 2.21×10^{-22} g, that is, as

$$2.21 \times \frac{1}{10\,000\,000\,000\,000\,000\,000\,000\,000}\ \mathrm{g}$$

Numbers such as 10^6 are called exponential numbers, where 10 is the *base* and 6 is the *exponent*. Numbers in the form 6.02×10^{23} are said to be written in *scientific notation.*

Table B-1
Positive powers of ten

$10^0 = 1$
$10^1 = 10$
$10^2 = 10 \times 10 = 100$
$10^3 = 10 \times 10 \times 10 = 1000$
$10^4 = 10 \times 10 \times 10 \times 10 = 10\,000$
$10^5 = 10 \times 10 \times 10 \times 10 \times 10 = 100\,000$
$10^6 = 10 \times 10 \times 10 \times 10 \times 10 \times 10 = 1\,000\,000$
|
$10^{23} = 100\,000\,000\,000\,000\,000\,000\,000$

Table B-2
Negative powers of ten

$10^{-1} = 1/10 = 0.1$
$10^{-2} = 1/100 = 0.01$
$10^{-3} = 1/1\,000 = 0.001$
$10^{-4} = 1/10\,000 = 0.000\,1$
$10^{-5} = 1/100\,000 = 0.000\,01$
$10^{-6} = 1/1\,000\,000 = 0.000\,001$
|
$10^{-13} = 1/10\,000\,000\,000\,000 = 0.000\,000\,000\,000\,1$

Exponential numbers are often used in calculations. The most common operations are multiplication and division. Two rules must be followed: (1) to *multiply* exponentials, *add* the exponents, and (2) to *divide* exponentials, *subtract* the exponents. These rules can be stated algebraically as

$$(x^a)(x^b) = x^{a+b}$$

$$\frac{x^a}{x^b} = x^{a-b}$$

Some examples follow.

$$(10^6)(10^4) = 10^{6+4} = 10^{10}$$
$$(10^6)(10^{-4}) = 10^{6+(-4)} = 10^{6-4} = 10^2$$
$$(10^{-5})(10^2) = 10^{(-5)+2} = 10^{-5+2} = 10^{-3}$$
$$(10^{-7})(10^{-3}) = 10^{(-7)+(-3)} = 10^{-7-3} = 10^{-10}$$
$$\frac{10^{14}}{10^6} = 10^{14-6} = 10^8$$
$$\frac{10^6}{10^{23}} = 10^{6-23} = 10^{-17}$$
$$\frac{10^{-10}}{10^{-6}} = 10^{(-10)-(-6)} = 10^{-10+6} = 10^{-4}$$
$$\frac{10^3}{10^{-2}} = 10^{3-(-2)} = 10^{3+2} = 10^5$$
$$\frac{10^{-8}}{10^4} = 10^{(-8)-4} = 10^{-12}$$
$$\frac{10^7}{10^7} = 10^{7-7} = 10^0 = 1$$

Problems involving both a coefficient (a numerical part) and an exponential are solved by multiplying (or dividing) coefficients and exponentials separately.

Example B-1 To what is the following expression equivalent?

$$(1.2 \times 10^5)(2.0 \times 10^9)$$

First, multiply the coefficients.

$$1.2 \times 2.0 = 2.4$$

Then multiply the exponentials.

$$10^5 \times 10^9 = 10^{5+9} = 10^{14}$$

The complete answer is

$$2.4 \times 10^{14}$$

Example B-2 To what is the following expression equivalent?

$$\frac{(8.0 \times 10^{11})}{(1.6 \times 10^{4})}$$

First, divide the coefficients.

$$\frac{8.0}{1.6} = 5.0$$

Then divide the exponentials.

$$\frac{10^{11}}{10^{4}} = 10^{11-4} = 10^{7}$$

The answer is

$$5.0 \times 10^{7}$$

Example B-3 Give an equivalent for the following expression.

$$\frac{(1.2 \times 10^{14})}{(4.0 \times 10^{6})}$$

It is convenient, before carrying out the division, to rewrite the dividend (the numerator) so that the coefficient is larger than that of the divisor (the denominator).

$$1.2 \times 10^{14} = 12 \times 10^{13}$$

Note that the coefficient was made larger by a factor of 10 and the exponential was made smaller by a factor of 10. The quantity as a whole is unchanged. Now divide.

$$\frac{12 \times 10^{13}}{4.0 \times 10^{6}} = 3.0 \times 10^{7}$$

Example B-4 Give an equivalent for the following expression.

$$\frac{(3 \times 10^{7})(8 \times 10^{-3})}{(6 \times 10^{2})(2 \times 10^{-1})}$$

In problems such as this, you can carry out the multiplications specified in the numerator and in the denominator separately and then divide the resulting numbers.

$$(3 \times 10^{7})(8 \times 10^{-3}) = 24 \times 10^{4}$$

$$(6 \times 10^{2})(2 \times 10^{-1}) = 12 \times 10^{1}$$

$$\frac{24 \times 10^{4}}{12 \times 10^{1}} = 2 \times 10^{3}$$

The multiplications and divisions in problems like this can be carried out in any convenient order.

There is only one other mathematical function involving exponentials that is of importance to us. What happens when you raise an exponential to a power? You just multiply the exponent by the power. To illustrate:

$$(10^{3})^{3} = 10^{9}$$

$$(10^{-2})^{4} = 10^{-8}$$

$$(10^{-5})^{-3} = 10^{15}$$

If the exponential is combined with a coefficient, the two parts of the number are dealt with separately, as in the following example.

$$(2 \times 10^{3})^{2} = 2^{2} \times (10^{3})^{2} = 4 \times 10^{6}$$

For a further discussion of—and more practice with—exponential numbers, see one of the following references.

1. Goldish, Dorothy M., *Basic Mathematics for Beginning Chemistry*, New York: Macmillan, 1975. Chapter 3 covers exponential notation.
2. Loebel, Arnold B., *Chemical Problem Solving by Dimensional Analysis*, Boston: Houghton Mifflin, 1974. Chapter 1, section A, deals with exponential notation.

appendix C

Solving Problems by Dimensional Analysis

A helpful method for solving problems like those encountered in this text is an approach called *dimensional analysis* or, sometimes, the *unit-factor method* or the *factor-label method*. The method employs the dimensions, or units, associated with a quantity as an aid in setting up the problem.

Quantities can be expressed in a variety of units. For example, you can buy beverages by the 12-oz can or by the pint, quart, gallon, or litre. If you wish to compare prices, you must be able to *convert* from one unit to another. To do this, one multiplies the original quantity by a *conversion factor*. Such a conversion changes the numbers and units involved but does not change the quantity. Your height, for example, is the same whether it is expressed in inches, feet, centimetres, or metres.

You know that multiplying a number by 1 doesn't change its value. Multiplying by a fraction equal to 1 also leaves the value unchanged. A fraction is equal to 1 when the numerator is equal to the denominator. For example, we know that

$$1 \text{ ft} = 12 \text{ in.}$$

Therefore, the fraction

$$\frac{1 \text{ ft}}{12 \text{ in.}} = 1$$

Similarly

$$\frac{12 \text{ in.}}{1 \text{ ft}} = 1$$

If we wish to convert from inches to feet we can do so by choosing one of the fractions as a conversion factor. *Which* one do we choose? The one that gives us an answer with the right units! Let's illustrate by an example.

Example C-1 My bed is 72 in. long. What is its length in feet?

Ignoring the smart alecks who immediately shouted out the answer, we shall proceed to show *how* the solution is obtained using the appropriate conversion factor. We need to multiply 72 in. by one of the above fractions. Which one? Let's try the first.

$$72\,\cancel{\text{in.}} \times \frac{1 \text{ ft}}{12\,\cancel{\text{in.}}} = 6 \text{ ft}$$

Note that the unit *inches* cancels, leaving us with an answer of 6 ft. Reasonable. A bed might well be 6 ft long. Just for kicks, though, let's try the other conversion factor.

$$72 \text{ in.} \times \frac{12 \text{ in.}}{1 \text{ ft}} = 864 \text{ in.}^2/\text{ft}$$

Absurd! How can a bed be 864 in.^{2}/ft?

You should have no difficulty choosing between the two possible answers.

Example C-2 A recipe calls for 74 ml of milk. You have a measuring cup which measures in fluid ounces. How many ounces of milk would you need? (1 fl oz = 29.6 ml.)

$$74\,\cancel{\text{ml}} \times \frac{1 \text{ fl oz}}{29.6\,\cancel{\text{ml}}} = 2.5 \text{ fl oz}$$

Notice that the unit millilitres must appear in the *denominator* of the conversion factor. (If you're not convinced, try it the other way.)

Example C-3 How many cubic centimetres of a penicillin preparation should be administered to a patient if the doctor's prescription specifies a dose of 600 000 units and the label on the penicillin container states that there are 150 000 units per cubic centimetre?

The 600 000 units must be converted to a value in cubic centimetres. The label gives the conversion factor (150 000 units = 1 cc).

$$600\ 000\,\cancel{\text{units}} \times \frac{1 \text{ cc}}{150\ 000\,\cancel{\text{units}}} = 4$$

By focusing on the units instead of the numbers, you can sometimes determine how to set up a problem.

Example C-4 A bottle filled to the 25-ml mark contains 75 g of bromine. What is the density of bromine?

If you know that density is ordinarily reported in grams per millilitre (chapter 1), then you know how to set up the problem. Arrange the data so the answer will come out in grams per millilitre. The density of bromine is

$$\frac{75 \text{ g}}{25 \text{ ml}} = 3 \text{ g/ml}$$

It is possible (and frequently necessary) to manipulate units in the denominator as well as the numerator of a problem. Just remember to use conversion factors in such a way that the unwanted units cancel.

Example C-5 At a track meet a runner completes the mile in 4 minutes. How fast is this in miles per hour?

$$\frac{1 \text{ mi}}{4\,\cancel{\text{minutes}}} \times \frac{60\,\cancel{\text{minutes}}}{1 \text{ hour}} = 15 \text{ mi/hour}$$

Example C-6 A sprinter runs the 100-yd dash in 10 seconds. How fast is this in miles per hour?

This problem calls for the manipulation of units in both the numerator and the denominator.

$$\frac{100\text{ yd}}{10\text{ seconds}} = x\text{ mi/hour}$$

Let us assume that we have no direct conversion factors between yards and miles or between seconds and hours. We'll set up the problem with the following factors.

$$3\text{ ft} = 1\text{ yd}$$
$$5280\text{ ft} = 1\text{ mi}$$
$$1\text{ minute} = 60\text{ seconds}$$
$$1\text{ hour} = 60\text{ minutes}$$

First, let's set up the factors which will convert yards to miles.

$$\frac{100\,\cancel{\text{yd}}}{10\text{ seconds}} \times \frac{3\,\cancel{\text{ft}}}{1\,\cancel{\text{yd}}} \times \frac{1\text{ mi}}{5280\text{ ft}} = x\text{ mi/second}$$

Next, let's incorporate the factors which will convert seconds to hours.

$$\frac{100\,\cancel{\text{yd}}}{10\,\cancel{\text{seconds}}} \times \frac{3\,\cancel{\text{ft}}}{1\,\cancel{\text{yd}}} \times \frac{1\text{ mi}}{5280\,\cancel{\text{ft}}} \times \frac{60\,\cancel{\text{seconds}}}{1\,\cancel{\text{minute}}} \times \frac{60\,\cancel{\text{minutes}}}{1\text{ hour}} = x\text{ mi/hour}$$

After carrying out all the indicated arithmetic we get the answer—20.5 mi/hour.

Here's one last problem just for fun.

Example C-7 If your heart beats 72 times per minute and your lifetime will be 70 years, how many times will your heart beat during your lifetime?

$$\frac{72\text{ beats}}{1\,\cancel{\text{minute}}} \times \frac{60\,\cancel{\text{minutes}}}{1\,\cancel{\text{hour}}} \times \frac{24\,\cancel{\text{hours}}}{1\,\cancel{\text{day}}} \times \frac{365\,\cancel{\text{days}}}{1\,\cancel{\text{year}}} \times \frac{70\,\cancel{\text{years}}}{1\text{ lifetime}}$$
$$= 2\,650\,000\,000\text{ beats/lifetime}$$

That's approaching 3 billion beats! Not bad for a bit of muscle the size of your fist!

For a more detailed discussion of this method of problem solving, consult one or more of the following sources.

1. Goldish, Dorothy M., *Basic Mathematics for Beginning Chemistry*, New York: Macmillan, 1975. Chapter 7 is entitled "Setting Up Problems: Dimensional Analysis."
2. Loebel, Arnold B., *Chemical Problem Solving by Dimensional Analysis*, Boston: Houghton Mifflin, 1974.
3. Zaborowski, Leon M., and Hill, John W., *Chemical Problems for Changing Times*, Minneapolis: Burgess, 1973.

appendix D

Answers to Selected Problems

Chapter 1

3. a. 20 °C; −3.9 °C; −23 °C
   b. −24 °F; 414 °F
   c. 310 K; 173 K
4. 50 000; 0.25; 23; 92
5. 10; 0.2; 142; 680
6. 1; 15
7. 1500 cal, or 1.5 kcal
8. 140 000 cal, or 140 kcal
9. 1.14 g/cm^3
10. 1.6 g/ml
11. 680 g
12. 1.02

Chapter 2

8. From 180 g of water, 20 g of hydrogen would be formed. To produce 2 t of hydrogen, 18 t of water are required. To produce 1 t of hydrogen, 9 t of water are required.
9. a. 30 g of carbon
   b. 300 g of carbon
10. There are four hydrogen atoms for each silicon.
17. $2n^2 = 2(4^2) = 32$ electrons

Chapter 3

2. a. 82 protons, 124 neutrons
   b. 1 proton, 2 neutrons
   c. 27 protons, 33 neutrons
   d. 90 protons, 143 neutrons
3. $^{24}_{12}\text{Mg} + {}^{1}_{0}\text{n} \rightarrow {}^{1}_{1}\text{H} + {}^{24}_{11}\text{Na}$
4. $^{215}_{85}\text{At} \rightarrow {}^{211}_{83}\text{Bi} + {}^{4}_{2}\text{He}$
5. $^{209}_{82}\text{Pb} \rightarrow {}^{0}_{-1}\text{e} + {}^{209}_{83}\text{Bi}$
6. After 4.5 seconds (one half-life), there were 1500 atoms left; after 9.0 seconds (two half-lives), there were 750 atoms left; after 13.5 seconds (three half-lives), there were 375 atoms left.

Chapter 4

4. a. LiF
   b. CaI_2
   c. $AlBr_3$
   d. $MgSO_4$
   e. $(NH_4)_3PO_4$
   f. $Na_2C_2O_4$
   g. $CaHPO_4$
   h. $Mg_3(PO_4)_2$
   i. KNO_3
   j. $Fe(OH)_3$
   k. Al_2S_3
   l. $Cu(CN)_2$
5. a. sodium bromide
   b. calcium chloride
   c. aluminum oxide
   d. calcium sulfate
   e. sodium hydrogen sulfate (sodium bisulfate)
   f. potassium hydrogen carbonate (potassium bicarbonate)
   g. magnesium acetate
   h. aluminum acetate
   i. ammonium phosphate
   j. ammonium oxalate
   k. potassium nitrite
   l. sodium monohydrogen phosphate
   m. potassium cyanide
   n. aluminum hydroxide
   o. calcium dihydrogen phosphate
   p. sodium carbonate
   q. magnesium hydrogen carbonate (magnesium bicarbonate)
   r. ammonium iodide
   s. calcium hydrogen sulfate (calcium bisulfate)
   t. sodium nitrate
7. a. bent
   b. tetrahedral
   c. linear
   d. planar

8.	$:\underset{\cdot\cdot}{\ddot{X}}\cdot$	$:\underset{\cdot}{\ddot{Y}}\cdot$	$:\underset{\cdot}{\dot{Z}}\cdot$
a.	VIIA	VIA	VA
b.	$:\underset{\cdot\cdot}{\ddot{X}}:H$	$:\underset{\ddot{H}}{\ddot{Y}}:H$	$:\underset{\ddot{H}}{\overset{H}{\ddot{Z}}}:H$
c.	linear (like HCl)	bent (like H_2O)	pyramidal (like NH_3)
d.	$:\underset{\cdot\cdot}{\ddot{X}}:^-$	$:\underset{\cdot\cdot}{\ddot{Y}}:^{2-}$	

Chapter 5

1. a. $4\,Al + 3\,O_2 \rightarrow 2\,Al_2O_3$
   c. $N_2 + O_2 \rightarrow 2\,NO$
   e. $2\,NO + O_2 \rightarrow 2\,NO_2$
   g. $Al_2(SO_4)_3 + 6\,NaOH \rightarrow 2\,Al(OH)_3 + 3\,Na_2SO_4$
   i. $3\,NH_4OH + H_3PO_4 \rightarrow (NH_4)_3PO_4 + 3\,H_2O$
2. a. 16
   c. 80
   e. 233
   g. 58
   i. 123
3. a. 2 moles
   c. 0.1 mole
   e. 0.001 mole
   g. 0.1 mole
   i. 0.03 mole
4. a. 0.016 g
   c. 4.0 g
   e. 699 g
   g. 336 g
   i. 2.46 g

5. a. 4 moles c. 1.6 g
   b. 16 g d. 10 ℓ
6. a. 32 g b. 96 kcal
10. a. The equilibrium would shift to the right.
    b. The equilibrium would shift to the right.
    c. The equilibrium would shift to the right.
    d. There would be no change in the equilibrium

Chapter 6

5. 200 ft^3
6. 1.25 ℓ
7. Oxygen will flow from flask A to flask B. Nitrogen will flow from flask B to flask A.
8. 40 psi
9. 3.3 ℓ
10. 12.7 ℓ
11. 431 ml
12. 22.2 ℓ/mole
13. 2.86 g/ℓ
14. 708 mm Hg
15. 50%

Chapter 7

8. 7200 cal/mole
10. 1 200 000 cal, or 1200 kcal
11. The calculated value is 7413 cal/mole; the experimental value from **table** 7.3 is 7300 cal/mole.
12. gold
13. 1000 cal
14. 72 250 cal, or 72.25 kcal

Chapter 8

2. a. 0 f. +3
   b. +6 g. +4
   c. −2 h. +4
   d. −1 i. +2
   e. +3 j. +6
3. a. $\boxed{Cl_2}\underline{KBr}$ e. $\underline{Fe}\boxed{HCl}$
   b. $\underline{Al}\boxed{O_2}$ f. $\boxed{HNO_3}\underline{SO_2}$
   c. $\boxed{C_2H_4}\underline{H_2}$ g. $\underline{C_2H_5OH}\boxed{MnO_4^-}$
   d. $\underline{SO_2}\boxed{O_2}$

Chapter 9

2. a. soluble h. soluble
   b. insoluble i. soluble
   c. soluble j. soluble
   d. soluble k. soluble
   e. insoluble l. insoluble
   f. insoluble m. insoluble
   g. soluble n. insoluble
   (See sections 9.3 and 9.4 for explanations.)
8. −1.86 °C; 100.51 °C; 101.02 °C
9. 6 moles; 0.6 mole; 0.006 mole
10. 1 g
11. a. Dissolve 5 g of NaOH in 95 ml of water.
    b. Dissolve 117 g of NaCl in water to give exactly 1 ℓ of solution as measured in a volumetric flask.
15. The dilution of 1:20 is more concentrated.

Chapter 10

6. hydrobromic acid
7. nitrous acid
8. oxalic acid
14. a. $Mg + 2\,HCl \rightarrow MgCl_2 + H_2$
    b. $HCl + LiOH \rightarrow LiCl + H_2O$
    c. $2\,Na + 2\,H_2O \rightarrow 2\,NaOH + H_2$

Chapter 11

1. a. 81, 81 e. 82, 27.3
   c. 34, 17 g. 60, 60
2. a. 0.5 *N* d. 0.4 *N*
   b. 1 *N* e. 2 *N*
   c. 1 *N*
3. 6 *N*
4. a. 2 ℓ b. 1.4 ml
5. a. 0.5 *N* b. 0.25 *N*
6. 0.125 *N*
7. a. 2 d. 11 f. 12
   b. 4 e. 5 g. 3
   c. 13
10. a. neutral d. basic
    b. basic e. acidic
    c. indeterminate f. neutral

Chapter 12

2. a. strong electrolyte f. nonelectrolyte
   b. strong electrolyte g. weak electrolyte
   c. weak electrolyte h. nonelectrolyte
   d. strong electrolyte i. strong electrolyte
   e. strong electrolyte
5. a. K and Br_2 b. Li and Cl_2 c. Al and O_2
10. $\underset{(Insoluble)}{CaCO_3} + 2\,HCl \rightarrow \underset{(Soluble)}{CaCl_2} + H_2O + CO_2$

Chapter 13

2. a. $:\underset{\cdot\cdot}{\overset{\cdot\cdot}{Ne}}:$ d. $\cdot K$
   b. $:\underset{\cdot}{\overset{\cdot\cdot}{O}}\cdot$ e. $\cdot\overset{\cdot}{Ba}$
   c. $:\underset{\cdot\cdot}{\overset{\cdot\cdot}{F}}\cdot$ f. $\cdot\underset{\cdot}{\overset{\cdot\cdot}{N}}\cdot$
7. a. $:\underset{\cdot\cdot}{\overset{\cdot\cdot}{F}}:^-$ d. $:\underset{\cdot\cdot}{\overset{\cdot\cdot}{S}}:^{2-}$
   b. $:\underset{\cdot\cdot}{\overset{\cdot\cdot}{I}}:^-$ e. K^+
   c. $:\underset{\cdot\cdot}{\overset{\cdot\cdot}{O}}:^{2-}$ f. Sr^{2+}
11. a. $4\,Li + O_2 \rightarrow 2\,Li_2O$ d. $CaO + H_2O \rightarrow Ca(OH)_2$
    b. $2\,Ca + O_2 \rightarrow 2\,CaO$ e. $SO_2 + H_2O \rightarrow H_2SO_3$
    c. $S + O_2 \rightarrow SO_2$ f. $Ca + S \rightarrow CaS$

Chapter 14

4. hexane; 2-methylpentane; 3-methylpentane; 2,3-dimethylbutane; 2,2-dimethylbutane
7. a. 3-methylhexane g. 1-pentyne
   b. 2-methyl-1-pentene h. 2,5-dimethyl-2-hexene
   c. methylcyclopropane i. 2-butyne
   d. cyclobutene j. 4-isopropylheptane
   e. ethylbenzene k. *m*-nitrotoluene
   f. *cis*-3-hexene l. 1,3,5-trinitrobenzene

Chapter 15

3. *n*-butyl chloride (common), or 1-chlorobutane (IUPAC); *sec*-butyl chloride (common), or 2-chlorobutane (IUPAC); isobutyl chloride (common), or 1-chloro-2-methylpropane (IUPAC); *tert*-butyl chloride (common), or 2-chloro-2-methylpropane (IUPAC)
5. a. 2-bromopentane e. 1,1,2-trichloroethane
   b. 3-chloro-2-methylhexane f. 1,2,4-tribromobenzene
   c. *m*-dichlorobenzene g. 2,4,6-trichloroheptane
   d. 1,1-dichloroethane
13. 30 g

Chapter 16

4. a. 2-hexanol
   b. di-*n*-propyl ether
   c. ethyl isopropyl ether
   d. *m*-chlorophenol (3-chlorophenol)
   e. *o*-bromophenol (2-bromophenol)

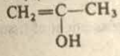
f. isobutyl alcohol (common), or 2-methyl-1-propanol (IUPAC)
g. isopropyl alcohol (common), or 2-propanol (IUPAC)
h. *n*-hexyl alcohol (common), or 1-hexanol (IUPAC)

6. a. ethanol
   b. methanol
   c. 2-propanol

13. a. oxidation
    b. dehydration
    c. oxidation
    d. hydration
    e. dehydration

Chapter 17

1. valeraldehyde (common), or pentanal (IUPAC); *β*-methylbutyraldehyde (common), or 3-methylbutanal (IUPAC); α-methylbutyraldehyde (common), or 2-methylbutanal (IUPAC); dimethylpropionaldehyde (common), or dimethylpropanal (IUPAC)
2. methyl *n*-propyl ketone (common), or 2-pentanone (IUPAC); diethyl ketone (common), or 3-pentanone (IUPAC); methyl isopropyl ketone (common), or 3-methyl-2-butanone (IUPAC)
3. a. benzaldehyde
   b. cyclopentanone
   c. ethyl isobutyl ketone, or 5-methyl-3-hexanone
   d. propionaldehyde, or propanal
   e. *β*,*β*-dimethylbutyraldehyde, or 3,3-dimethylbutanal

9.


$$CH_2{=}\underset{\displaystyle OH}{\underset{|}{C}}{-}CH_3$$

Chapter 18

1. a. formic acid (common), or methanoic acid (IUPAC)
   b. propionic acid (common), or propanoic acid (IUPAC)
   c. α,γ-dimethylvaleric acid (common), or 2,4-dimethylpentanoic acid (IUPAC)
   d. capric acid (common), or decanoic acid (IUPAC)
   e. glutaric acid (common), or pentanedioic acid (IUPAC)
2. a. sodium benzoate
   b. calcium propionate
   c. ammonium acetate
   d. zinc butyrate
   e. calcium phthalate
5. a. *n*-propyl propionate
   b. N-isopropylacetamide
   c. isobutyl benzoate
   d. phenyl butyrate
   e. benzamide
   f. butyranilide

Chapter 19

1. *n*-butylamine (1°); *sec*-butylamine (1°); isobutylamine (1°); *tert*-butylamine (1°); methyl-*n*-propylamine (2°); methylisopropylamine (2°); diethylamine (2°); dimethylethylamine (3°)
10. a. mixture
    b. single compound
    c. single compound
    d. single compound
    e. mixture
    f. single compound
    g. mixture of two isomers
    h. single compound
13. 350 mg (0.35 g, or about 0.01 oz)

Chapter 20

2. a. propanethiol, or *n*-propyl mercaptan
   b. methanesulfonic acid
   c. dimethyl sulfoxide
   d. diethyl sulfone
   e. diethyl disulfide
   f. ethyl methyl sulfide
   g. pyrophosphoric acid
   h. trimethylphosphine
   i. ethyl dihydrogen phosphate
   j. *o*-chlorobenzenesulfonamide

Chapter 21

3. All are made from cellulose.
5. a double bond
13. acrylonitrile and styrene

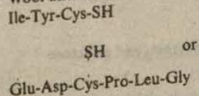
Chapter 22

7. a. glucose
   b. glucose
   c. glucose
   d. glucose, galactose
   e. fructose, glucose
9. a. glucose
   b. lactose
   c. sucrose
   d. glucose
   e. fructose
   f. fructose, glucose
   g. sucrose
10. a. α-D-galactose
    b. α-D-glucose
    c. alpha linkage
    d. yes; alpha linkage
11. a. beta
    b. no—the first carbon is fixed as an acetal, not as a hemiacetal
    c. no; no

Chapter 23

9. tristearin in both cases
11. a. saponifiable
    b. nonsaponifiable
    c. saponifiable
    d. nonsaponifiable
    e. neither
    f. sphingosine
    g. neither
12. a. glycerol
    b. glycerol
    c. neither
    d. glycerol
13. Only the phosphatides (d) contain phosphate units.

Chapter 24

6. Three problems associated with a strict vegetarian diet are that such a diet is likely to be lacking in some essential amino acid, that vitamin B_{12} cannot be obtained from plant products, and that calcium, iron, riboflavin, and other vitamins may be inadequately supplied.
7. The secondary structure of silk is termed the *pleated sheet* conformation.
10. The secondary structure of wool has been given the designation *alpha helix*.
12. Wool and silk are fibrous proteins. Myoglobin is a globular protein.
13.


Ile-Tyr-Cys-SH

SH

Glu-Asp-Cys-Pro-Leu-Gly

or Cys-Tyr-Ile-Glu-Asp-Cys-Pro-Leu-Gly; no

Chapter 25

1. a. For DNA, the bases are adenine and guanine (purines) and cytosine and thymine (pyrimidines); for RNA, the bases are adenine and guanine (purines) and cytosine and uracil (pyrimidines).
   b. For DNA, the sugar is deoxyribose; for RNA, the sugar is ribose.
   c. uracil and ribose
2. a. adenine and ribose
   b. guanine and deoxyribose
   c. uracil and ribose
   d. cytosine and ribose
3. Compound I is a nucleoside and a pyrimidine and is incorporated in DNA. Compound II is a nucleotide and a purine and is incorporated in RNA.

Chapter 26

4. Enzymes do not change the extent of a reaction; they merely change the speed with which the equilibrium concentrations can be reached. Enzymes catalyze the forward *and* the reverse reaction. (See section 26.4.)
5. All enzymes are proteins. Some require metal ions or organic cofactors in order to carry out their catalytic function.
10. EDTA chelates the lead ions, and this complex can be excreted from the body. (See section 26.9.)
11. Cyanide reacts with cytochrome oxidases by tying up the electrons which these enzymes normally supply in reduction reactions. The deactivation of the oxidases prevents reduction of oxygen in the cell, which means that cell respiration is interrupted. (See section 26.9.)
12. Thiosulfate converts the cyanide ion to the relatively nontoxic thiocyanate ion. (See section 26.9.)

Chapter 27

4. Many vitamins are changed in the body to active coenzymes. (See section 27.6 and table 27.2.)
5. Synthetic and natural vitamin C are identical. All vitamin C is ascorbic acid.
6. Water-soluble vitamins would be lost. They would be extracted by the water in which the vegetables were cooked and then lost when this water was poured off.
8. A critical event in the visual process involves the isomerization of one isomer of vitamin A (*cis*-retinal) to another (*trans*-retinal). (See section 27.2.)
10. Vitamin A and polyunsaturated fatty acids are believed to be protected from oxidation by the presence of vitamin E. (See section 27.4.)

11. The B complex is the group of water-soluble vitamins commonly found together in a variety of food sources. They are not closely related structurally. (See section 27.6 and **table 27.1.**)

Chapter 28

3. Ca^{2+}
6. albumins, globulins, fibrinogen, prothrombin
7. Na^+, K^+, Ca^{2+}, and Mg^{2+} are positive ions; HPO_4^{2-}, Cl^-, HCO_3^-, and SO_4^{2-} are negative ions.
8. a. $Cl^- = 120$ meq/ℓ; $Ca^{2+} = 1.25$ meq/ℓ; $Na^+ = 140$ meq/ℓ.
   b. Concentrations of chloride ion and sodium ion are normal; concentration of calcium ion is significantly below normal.
13. The main blood buffers are the bicarbonate/carbonic acid system, the monohydrogen phosphate/dihydrogen phosphate system, and the plasma proteins.
17. When bicarbonate ion diffuses from red blood cells, chloride ion diffuses into these cells to maintain electrical neutrality. (See section 28.5.)
26. The lymphatic system returns components of interstitial fluid to the blood circulation, carries fats from the intestines to the blood circulation, is the site of white blood cell and antibody synthesis, and serves as a filtering system to remove dead cells and bacteria from circulation.
28. The volume of urine excreted is affected by liquid intake, body temperature, amount of perspiration, and other liquid losses (e.g., because of diarrhea).
29. Three organic components of urine are urea, uric acid, and the breakdown products of bilirubin. In certain pathological conditions, glucose (blood sugar) is also present.

Chapter 29

10. Gallstones are usually chiefly cholesterol.
11. a. monosaccharides, including glucose, fructose, and galactose
    b. monoglycerides and fatty acids
    c. amino acids
12. Fats are absorbed through the villi and into the lymphatic system rather than directly into the blood.
13. a. flow initiated by the protein hormone gastrin
    b. flow initiated by the protein hormone secretin
    c. the release of bile stored in the gallbladder signaled by the protein hormone cholecystokinin

Chapter 30

3. Glucose in the urine does *not* always indicate diabetes mellitus. (See section 30.2.)
4. Insulin is a peptide and will, if taken orally, be subjected to and deactivated by the same digestive enzymes which hydrolyze protein foods.
5. The oral drugs are nonprotein and act to stimulate the production of insulin by the pancreas. (See section 30.2.)
7. Glycogen synthetase is responsible for forming the 1,4 linkages, and the branching enzyme forms the 1,6 linkages in glycogen. (See section 30.3.)
8. lactic acid
9. Step 6 in the Embden-Meyerhof pathway involves the oxidation of glyceraldehyde-3-phosphate to 1,3-diphosphoglyceric acid. The oxidizing agent is NAD^+.
12. The Krebs cycle provides energy to the cell in the form of energy-rich ATP molecules. (See section 30.5.)
13. as two carbon dioxide molecules
14. NAD^+ and FAD

Chapter 31

2. Lipids and fatty acids are ordinarily complexed with water-soluble proteins to form lipoproteins. The lipoproteins are readily transported by the blood.
3. acetyl coenzyme A
4. Acetyl coenzyme A serves as fuel for the Krebs tricarboxylic acid cycle, as a starting material for fatty acid synthesis, and as a starting material for steroid synthesis.
5. The glycerol can enter the glycolysis pathway (Embden-Meyerhof pathway) after being phosphorylated and then oxidized to dihydroxyacetone phosphate. (See section 31.3.)
9. overeating—eating more food than is required for replacement of tissue and for energy needs
10. Cytidine triphosphate acts as a carrier molecule. It combines with one reactant molecule and activates it for transfer to a second reactant. (See section 31.6 for examples.)
11. cholesterol
13. During a fast, glycogen reserves are used first, fat reserves supply the major part of the body's needs, and proteins, including ultimately structural protein such as that of muscle, are called on as a final source.
18. 130 ATP

Chapter 32

3. Breakdown of dietary protein, breakdown of tissue protein, and synthesis of amino acids would all add to the amino acid pool. Synthesis of proteins, synthesis of nitrogen-containing nonprotein molecules, and catabolism of amino acids to produce energy would all deplete the amino acid pool.
4. a. The person goes into negative nitrogen balance.
   b. The person goes into negative nitrogen balance.
   c. The person goes into positive nitrogen balance.
6. a. aspartic acid b. alanine c. phenylalanine

Index

Abortifacient, 490, 566
ABS detergent, 432
Absolute temperature scale, 12, 135
Absolute zero, 12
Accelerators, 55
Acetaldehyde, 372, 608
Acetal linkage, in sugars, 465
Acetals, 367-68
Acetaminophen, 392
Acetanilide, 392
Acetic acid, 377
Acetic anhydride, 387
Acetoacetic acid, 630, 642
Acetoacetyl coenzyme A, 624, 642
Acetone, 630
Acetylcholine, 437-38
Acetyl coenzyme A, 608ff, 621ff, 633, 641
  structure of, 609
Acetylsalicylic acid, 384, 388-89
Acidic oxides, 263
Acidosis, 236, 576, 631
Acids
  Arrhenius theory of, 206
  Brønsted-Lowry theory of, 217
  effect of on tissue, 220
  inorganic nomenclature of, 209
  relative strengths of, 219
Aconitase, 610
Aconitic acid, 348, 610
Acrolein, 476
ACTH, 561, 602
Activation energy, definition of, 116
Active site, 536-37
Active transport, 491, 590-91
Activity series of metals, 212-13
Actomyosin, 614-15
Addition polymerization, 442
Adenine, 516, 648-49
Adenosine, 518
Adenosine diphosphate (ADP), 520, 605
Adenosine monophosphate (AMP), 519, 621
  cyclic, 520
Adenosine triphosphate (ATP), 520, 605
  in metabolic reactions, 604, 606-7, 610, 613-15, 621-24, 628-30
Adenylic acid, 519
Adipose tissue, 619
ADP, 520, 605
Adrenalin (epinephrine), 409, 561, 602
Adrenocorticotropic hormone (ACTH), 561, 602
Air, composition of, 127-28
Alanine, 641, 644
β-Alanine, 649, 651
Albinism, 645
Albumin, 511, 572
Alchemy, 2
Alcohol. *See* Ethyl alcohol
Alcohol dehydrogenase, 534, 540
Alcohols, 337-52
  chemical properties of, 347-50
  nomenclature of, 338-41
  physical properties of, 341-42
  physiological properties of, 345-47
Aldehydes, 358-74
  nomenclature of, 359-62
  physical properties of, 363-64
Aldolase, 606
Aldol condensation, 371-72, 606, 610
Aldosterone, 561
Aldrin, 328
Alkali metals, 272-74
Alkaline earth metals, 274-75
Alkaloids, 414-18
Alkalosis, 236, 576
Alkanes, 281-97
  chemical properties of, 297
  nomenclature of, 286-92
  physiological properties of, 296-97
Alkenes, 298-305
  chemical properties of, 304-5
  nomenclature of, 298-303
  physiological properties of, 303-4
Alkylbenzenesulfonate (ABS) detergent, 432
Alkyl group, definition of, 315
Alkynes, 305-6
Allantoin, 651
Allosteric site, 540
Allotropes, 263
Alpha decay, 50
Alpha helix, 509-10
Alpha particles, 257
Alpha rays, 33
Amides, 376, 391-97
  chemical properties of, 397
  nomenclature of, 391-92
  physical properties of, 394
Amines, 400-424
  chemical properties of, 405-9
  nomenclature of, 401-4
  physical properties of, 405
Amino acid pool, 637-38

Amino acids, 493-503
  biosynthesis of, 643-46
β-Aminoisobutyric acid, 649, 651
Aminopeptidase, 536, 590
Ammonia, 95-96, 210
Amobarbital, 414
AMP. *See* Adenosine monophosphate
Amphetamine, 410-12
α-Amylase, 588, 592
Amylopectin, 469, 602
Amylose, 469
Anabolism, 637
Andersen, Kenneth, 426
Androgens, 562
Anemia, 570
Anesthetics, 417, 419-20
Anions, 30
Anode, 27, 239
Antacids, 216-17
Antibodies, 575
Anticodon, 529
Antigens, 575
Antiseptics, 178-79
Apoenzyme, 541
Apothecary weights, 9
Arginase, 535, 540
Arginine, 535, 595, 647
Argininosuccinic acid, 647
Argon, 258
Aromatic compounds, nomenclature of, 309
Aromatic hydrocarbons, 307-11
  physiological properties of, 311
Arrhenius, Svante, 206, 242
Arsenic poisoning, 542
Arteriosclerosis, 477-78
Artificial transmutation, 53-54
Aryl group, definition of, 315
Ascorbic acid (vitamin C), 556-58
Aspartic acid, 641, 644-45, 647
Aspirin, 384, 388-89
Atmosphere (unit of pressure), 130
Atom
  Dalton's definition of, 22
  Greek view of, 17
  raisin pudding model of, 29, 30, 34-35
Atomic bomb, 71
Atomic mass unit (amu), 23
Atomic number, 48-49
Atomic symbols, 23-24
Atomic theory, 21-22
Atomic weight, 51
Atomistic theory of matter, 17, 21-22
ATP. *See* Adenosine triphosphate
Atropine, 436-37
Autocatalysis, 540
Autoclave, 153-54
Autoradiograph, 64
Avogadro, Amadeo, 107
Avogadro's number, 110
Background radiation, 59
Bacon, Sir Francis, 2
Bacteria, role of in digestion, 593-95
Baeyer, Adolph von, 413
Bakelite, 447-48
BAL, 427, 542
Barbital, 413
Barbiturates, 413-14
Barbituric acid, 413
Barium sulfate, use of in X-ray diagnosis, 249
Base pairing, in nucleic acids, 521-23
Bases, 210
  effect of on tissue, 220
  relative strengths of, 219
Basic oxides, 262
Batteries, 246-48
Becquerel, Antoine Henri, 32-33
Beeswax, 482
Bends, 141
Benedict's reagent, 464
Benzaldehyde, 373
Benzedrine (amphetamine), 410-12
Benzene, 307-8
Benzocaine, 384, 418
Benzpyrene, 310
o-Benzyl-*p*-chlorophenol, 353
Beriberi, 548
Bernstein, David, 426
Berylliosis, 275
Berzelius, J. J., 19, 22-23
Beta decay, 50
Beta oxidation, 622
Beta rays, 33
Biacetyl, 373
Bicarbonates, reaction of with acids, 214-15
Bilayers, 490-91, 619
Bile, 592-93
Bile salts, 487, 593
Bilifuscins, 595
Bilirubin, 579, 595
Binding energy, 75-76
Biochemical oxygen demand (BOD), 191
Biotin, 554, 556, 595
Birth control pill, 563-66
bis(Chloromethyl)ether, 355
Bleaches, 179-80
Blood, 569-78
Blood buffers, 235, 576-77
Blood cells, 570
Blood clotting, 544-45, 553
Blood sugar, 461
Bohr, Niels, 38-40, 42-44, 68
Boiling point, 153-54
  elevation of, 197, 241-42
Bonding
  covalent, 89ff
  ionic, 85ff
  polar covalent, 91ff
Botulinus, 437
Boyle, Robert, 18-19, 130
Boyle's law, 130-34
Bradykinin, 505
Branching enzyme, 603
Breathing, mechanics of, 133
Breeder reactors, 75
British Anti-Lewisite (BAL), 427, 542
British system of measurement, 9
Bromine, 260
Brønsted, J. N., 217
Buffers, in blood, 235, 576-77
Buffer solution, 233
Butacaine, 418, 420
Butenandt, Adolf, 563
Butesin, 418
Butesin picrate, 418
Butyric acid, 378

Cadaverine, 405, 595
Caffeine, 416
Calciferol, 550-51
Calcium phosphate, in bones and teeth, 251
Caloric, 19
Calorie, 12-13
Camphor, 373
Canfield, Robert, 533
Carbamyl phosphate, 646-47
Carbanion, 371
Carbohydrase, 534
Carbohydrate metabolism, 597-616
Carbohydrates, 458-72
Carbolic acid, 179, 352
Carbon
  allotropes of, 270
  properties of, 270
Carbonates, reaction of with acids, 214-15
Carbon dioxide
  and hemoglobin transport, 576-77
  pollution, 271-72
Carbon monoxide
  poisoning, 141, 144, 613
  pollution, 270-71
Carbon tetrachloride, 316
Carbonyl group, 358
Carbowax, 483
Carboxyl group, 375-76
Carboxylic acids, 375-83
  chemical properties of, 381-83
  nomenclature of, 376-80
  physical properties of, 380-81
Carboxypeptidase, 536, 591
Carisoprodol, 421
Carlisle, Anthony, 27, 238
Carnauba wax, 483
β-Carotene, 548
Carson, Rachel, 324
Casein, 583
Catabolism, 637

Catalyst
  definition of, 121
  role of in hydrogenation, 172
Catenation, 280
Cathode, 27, 239
Cathode ray, 27
Cation, 30
Cell membranes, 490-91
Cellophane, 441
Celluloid, 441
Cellulose, 470-71
Cellulose acetate, 441
Celsius scale, 11
Centigrade scale, 11
Cephalin, 484, 627-28
Cesium-137, 73
Chadwick, James, 36, 54
Chain reaction, nuclear, 68, 74
Charges, electrical, 7
Chargoff, Erwin, 521
Charles, J. A. C., 134
Charles' law, 134-36
Chemical properties, definition of, 26
Chemistry, definition of, 5
Chloral hydrate, 325, 367
Chloramphenicol, 369
Chlordane, 328
Chlordiazepoxide, 420-21
Chlorine, 179, 260
Chloroform, 316, 319, 331-32, 417
Chlorpromazine, 421-22
Cholecystokinin, 592
Cholesterol, 337, 487, 634
  biosynthesis of, 633
Cholic acid, 487, 634
Choline, 437-38
Cholinesterase, 437-38
Chromosomes, 524-25
Chyme, 589, 591
Chymotrypsin, 537, 591
Chymotrypsinogen, 591
Cinnamaldehyde, 373
Cis-trans isomerism. *See* Geometric isomerism
Citric acid, 348, 609-10
Citric acid cycle (Krebs cycle), 608-12, 642
Citrulline, 647
Cobalt-60, 63
Cocaine, 416-19
Codon, 529
Coenzyme, definition of, 540-41
Coenzyme A, 556
Coenzymes, table of, 556
Cofactor, 540
Cohen, Maimon, 396
Collagen, 510-11, 544
Colloid, definition of, 201
Colloidal dispersions, 201-2
Colloid osmotic pressure, 574
Combined gas laws, 137-38
Combining volumes, law of, 106-9
Compound, definition of, 19, 24
Concentration
  in milliequivalents per litre, 571-72
  in milligram percent, 196
  in molarity, 193
  in normality, 224
  in parts per billion, 196
  in parts per million, 196
  in percent by volume, 194
  in percent by weight, 195
Condensation, 152
Condensation polymerization, 442
Configuration, electronic, 40-41
Coniine, 416
Conjugate acid-base pair, 218
Conservation of mass, law of, 18, 22
Constant composition, law of, 20
Continuous spectrum, 37
Continuous theory of matter, 17, 21
Contraceptives, 563-66
Control rods, 74
Copolymerization, 449-50
Cori, Carl, 603
Cori, Gerty, 603
Cori cycle, 603-4, 608
Corticosterone, 634
Cortisol, 561, 602
Cortisone, 562, 602
Cosmic rays, 55
Cotinine, 372
Coumarin, 384
Covalent bonding, 89ff
Covalent network crystals, 158
CPK, 545, 615, 645
Cracking, of petroleum, 293-94
Creatine, 615
Creatine phosphate, 615
Creatine phosphokinase (CPK), 545, 615, 645
Crenation, 200
Crick, Francis, 522-23
Critical mass, 71
Crookes, William, 27-29
Crystal lattice, 156
Crystal types, 157-58
Curare, 417, 437
Curie, Marie Sklodowska, 33, 55, 604
Curie, Pierre, 33, 55, 604
Curie (unit of radiation), 56
Cyanide poisoning, 541, 613
Cyanocobalamine, 555-56
Cyclic adenosine monophosphate (cyclic AMP), 520
Cycloalkanes, 306-7
Cyclopropane, 417
Cysteine, 543, 644
Cytidine, 518
Cytidine phosphates, 628-30
Cytidylic acid, 519
Cytochrome oxidase, 541
Cytochromes, 613
Cytosine, 516, 649, 651

Dacron, 450, 453
Dalton, John, 20-24, 27-30, 44, 107, 139
Dalton's law of partial pressures, 139-40
Davy, Sir Humphrey, 238
DDT, 322ff
De Broglie, Louis, 42
Decarboxylase, 534
Definite proportions, law of, 20, 22, 26
Dehydration, 347
7-Dehydrocholesterol, 550-51
Dehydrogenases, 534
Deliquescence, 187
Democritus, 16, 17, 22
Denaturation, 512-13
Denatured alcohol, 346
Density, 13
  of a gas, 138
Deoxycholic acid, 487
Deoxyguanosine, 518
Deoxyribonucleic acid (DNA), 516, 521-23
  replication of, 524-26
Deoxyribonucleoside, 517
Deoxyribose, 460-61, 517
Deoxythymidine, 518
DES, 566-67
Destructive distillation, 338-39
Detergent action, 480-81
Detergents, 431-33
Deuterium, 48, 77
Dexedrine, 411-12
Dextrins, 469
Dextrose, 461
Diabetes mellitus, 581, 599, 600, 631
Dialysis, 203-4
Diamond, 270
Diazepam, 420-21
p-Dichlorobenzene, 318
Dichlorodiphenyltrichloroethane (DDT), 322ff
2,4-Dichlorophenoxyacetic acid, 331
Dieldrin, 328
Diethyl ether, 354-55, 417
Diethylstilbestrol (DES), 566-67
Digestion, 586-96
Digestive tract, 586-87
Dihydroxyacetone, 372, 459-60
Dihydroxyacetone phosphate, 606-7, 620-21
3,3-Dimethylallyl pyrophosphate, 633
Dimethyl sulfoxide (DMSO), 430
Dioxins, 331-32
Dipeptidase, 534, 590
Dipole, 94
Dipole forces, 148-49
Diprotic acids, 207

Disaccharides, 459, 466-68
Disinfectants, 179
Dispersion forces, 149-50
Dissociation, 242
Distillation, 154-55
Disulfide linkages, protein, 507
Disulfides, 429
Divinyl ether, 417
Djerassi, Carl, 563, 565
DMSO, 430
DNA. *See* Deoxyribonucleic acid
Double helix, 522
D series of sugars, 460

Edema, 574
EDTA, 542-43
Efflorescence, 187
Eijkman, Christiaan, 548
Einhorn, Alfred, 419
Einstein, Albert, 5, 18, 68
Electrical nature of atom, 27
Electrocardiograph, 248
Electrodes, 27, 239
Electroencephalograph, 248
Electrolysis, 239, 243-45
Electrolytes, 238-55
  in blood, 571-72
  definition of, 240
Electron, 27, 48
Electron dot symbols, 82ff
Electronegativity, 92-93
Electron transport system, 613
Electrophoresis, 499
Element
  Boyle's definition of, 19
  Dalton's definition of, 24
  Greek view of, 17
  modern definition of, 42
Elements, symbols for, 24
Embden, Gustav, 607
Embden-Meyerhof pathway (glycolysis), 604-8
Emphysema, 220
Emulsifying agents, 203
Endothermic reaction, 115
End point of titration, 226
Endrin, 328
Energy
  changes in during chemical reactions, 114ff
  definition of, 6
  and heat, 12
Energy level, electronic or atomic, 38-40, 43
Enterokinase, 540, 590-91
Enzyme activity
  effect of concentration on, 537-38
  effect of pH on, 538-39
  effect of temperature on, 539
Enzymes, 122, 532-46
  classification of, 534
  commercial use of, 544-46
  optimum pH for, 538
  optimum temperature for, 539
  specificity of, 535-36
Epinephrine, 409, 561, 602
Equations, chemical, 103ff
Equilibrium
  in chemical reactions, 123ff
  liquid-vapor, 152-53
  in saturated solutions, 189
Equivalence point, 226-27
Equivalent weight, 224
Ergosterol, 550-51
Erythrocytes, 570
Essential amino acids, 498, 638-39, 643-44
Esters, 376, 383-91
  chemical properties of, 390-91
  nomenclature of, 383-86
  physical properties of, 386
Estradiol, 563
Estrogens, 562-63
Estrone, 563, 634
Ethanol. *See* Ethyl alcohol
Ethanolamine, 628
Ethers, 353-55
  nomenclature of, 353
  properties of, 353-55
Ethisterone, 563, 565
Ethyl alcohol, 343-44, 346-47, 608
Ethylenediaminetetraacetic acid (EDTA), 542-43
Ethylene glycol, 351
Evaporation, 4
Exothermic reaction, 115

Factor X_a, 545
FAD, 556, 611-13, 622
Fahrenheit scale, 11
Fallout, radioactive, 61, 71-74
Faraday, Michael, 27, 307
Farnesyl pyrophosphate, 633
Fat depots, 619
Fats, 475-79
  biosynthesis of, 626-27
  saturated, 475-76
  unsaturated, 477-78
Fat-soluble vitamins, 548-53
Fatty acid cycle, 621
Fatty acids, 474-75
  biosynthesis of, 623-26
Feces, 595-96
Feedback inhibition, 540
Fehling's reagent, 464-65
Fermentation, 343-44, 608
Fermi, Enrico, 68
Fertilizers, 266
Fibrin, 545
Fibrinogen, 545, 572
Fibroin, 508
Film badges, 59
Fission, nuclear, 68, 77
Flavin adenine dinucleotide (FAD), 556, 611-13, 622
Flavin mononucleotide (FMN), 556
Fluorescence, 32
Fluoride salts, 260
Fluoroacetic acid, 610
FMN, 556
Folic acid, 554, 556
Follicle-stimulating hormone (FSH), 561
Food calorie, 13
Force, definition of, 7
Formaldehyde, 372
Formed elements of blood, 570
Formic acid, 377, 381
Franklin, Benjamin, 238
Freezing point, depression of, 197, 241-42
Freons, 321
Frisch, Otto, 68
Fructose, 372, 461, 468
Fructose 1,6-diphosphate, 606
Fructose 6-phosphate, 598, 606
FSH, 561
Fumarase, 612
Fumaric acid, 611-12, 642, 647-48
Functional group, 336
Funk, Casimir, 548
Fusion, 158-59
  heat of, 158
Fusion, nuclear, 76-78

Galactose, 461-62, 467
Galactosemia, 583, 599
Gallstones, 487, 593, 595
Gamma decay, 51
Gamma globulins, 575, 584
Gamma rays, 33
Gangliosides, 486
Gangrene, 142
Gases, 6, 127-45
  effect of pressure on solubility of, 192
Gas laws, 130-34, 134-36, 136-37, 139, 141
Gastric juice, 588
Gastrin, 588
Gaucher's disease, 635
Gay-Lussac, Joseph Louis, 107, 136
Gay-Lussac's law, 136-37
GDP, 611
Geiger counter, 58
Gelatin, 510
Genes, 524
Genetic code, 529
Geometric isomerism, 301-3
  and chemistry of vision, 548-50
Glacial acetic acid, 381
Globin, 579
Globular proteins, 511

Globulins, 511, 572
Glucagon, 561, 601–2
Glucose, 337, 461, 467–68, 599, 600, 606
Glucose 1-phosphate, 599
Glucose 6-phosphate, 606
Glucose tolerance test, 601
Glutamic acid, 640–41, 643–45
Glutamic-oxaloacetic transaminase (GOT), 545, 645
Glutamine, 644
Glutathione, 503–4
Glyceraldehyde, 372, 459–60
Glyceraldehyde 3-phosphate, 606–7
Glycerol, 351, 475–76, 624
Glycerol phosphate, 620, 626
Glyceryl tristearate, 384
Glycine, 644
Glycine oxidase, 539
Glycogen, 470, 599, 600, 602–3, 619
Glycogenesis, 603
Glycogenolysis, 603
Glycogen synthetase, 602
Glycolic acid, 454
Glycolipids, 485–86, 635
Glycols, 350–52
Glycolysis, 604–8
Glycoside, 465
Goiter, 253
Gold foil experiment, 34, 64
Goldstein, Eugen, 28–30, 36, 54
GOT, 545, 645
Gout, 651
Grain alcohol, 343
Gram, 9
Graphite, 270
Gravity, definition of, 7
Greenhouse effect, 272
GTP, 611
Guanine, 516, 649
Guanosine diphosphate (GDP), 611
Guanosine triphosphate (GTP), 611
Guanylic acid, 519

Haber, Fritz, 3, 268
Haber process, 2–3, 267–68
Hahn, Otto, 68
Half-life, 52–53
Halocarbons, 313–34
    physical properties of, 318–19
    physiological properties of, 319–20
Halogens, 259–61
Halothane, 319, 419
Hard water, 275, 481–82
Heat capacity, 160, 162
Heat energy, 12
Heat of fusion, 158
Heat of vaporization, 155
Helium, 257–58
Heme, 511, 577
Hemiacetals, 367–68
    in sugars, 465
Hemoglobin, 144, 253, 271, 276, 576–79
Hemolysis, 199
Hemophilia, 544–45
Henry, William, 141
Henry's law, 141
Heptachlor, 328
Heroin, 389–90
Hess, Victor Franz, 55
Heterocyclic compounds, 412
Hexachlorophene, 331–32, 353
cis-3-Hexenal, 373
4-*n*-Hexylresorcinol, 353
HGH, 561, 602
Histamine, 588, 594
Histidine, 594
Hofmann, Albert, 395
Homologous series, 281
Hopkins, F. G., 548
Hormones, 558–67
Human growth hormone (HGH), 561, 602
Humidity, 140–41
Hydrate, 187
Hydrates, of aldehydes and ketones, 366–67
Hydration, 185, 305
Hydride ion, 89
Hydrocarbons, 279–312
    saturated, 281
    unsaturated, 298
Hydrochloric acid, 216, 220, 588
Hydrogen, 171–73
Hydrogenation, 304–5
    of polyunsaturated fats, 478
Hydrogen bomb, 77
Hydrogen bond, 149
Hydrogen bonding
    in aqueous solutions, 187ff
    and base pairing in nucleic acids, 522–23
Hydrogen ion, 206–7
Hydrogen peroxide, 176–78, 180
Hydrolase, 534
Hydrometer, 14
Hydronium ion, 207
Hydrophobic interactions, 507–8
Hydroxide ion, 210
β-Hydroxybutyric acid, 630
Hydroxyl group, 336
Hygroscopicity, 187
Hyperbaric chamber, therapeutic uses of, 141–42
Hyperglycemia, 599
Hypertonic solutions, 200
Hyperventilation, 576
Hypoglycemia, 599
Hypotonic solutions, 199
Hypoxanthine, 648–49
Imidazole, 412
Imine, 369
Imipramine, 421–22
Immune response, 575
Immunoglobulins (gamma globulins) 575, 584
Indicator dyes, 230
Indole, 412, 594
Inhoffen, Hans, 563
Inorganic chemistry, definition of, 2
Insulin, 532, 561, 600–601
Interionic forces, 150–51
International system of measurement, 9
Intestinal juice, 589–90
Intrinsic factor, 589
Invert sugar, 468
Iodine, 253, 260–61
Iodine number, 476–77
Iodine-131, 65, 72
Ion, definition of, 30
Ionic bonding, 84ff
Ionic bonds, 150–51
Ionic compounds, nomenclature of 86–89
Ionic solids, 157–58
Ionization, 243
Ionizing radiation, 57
Ion product of water, 228
Ions
    complex, 100–101
    electronic configurations of, 81
Irone, 373
Iron lung, 133–34
Isocitric acid, 349, 610–11
Isoelectric point, 499, 502
Isomerase, 534
Isomerism
    definition of, 282
    geometric, 301–3
Isooctane, 294
Isopentenyl pyrophosphate, 633
Isoprene, 448
Isotonic solution, 200
Isotope, definition of, 48
Isotopes, 41
    symbols for, 49
IUPAC nomenclature, 286–92

Jaundice, 595
Joliot-Curie, Frédéric, 33, 54–55,
Joliot-Curie, Irène, 33, 54–55, 60
Jolles, Pierre, 533

Kekulé, Friedrich August, 307, 4
Kelvin temperature scale, 12, 13
Kepler, Johannes, 39
Ketal, 368
Keto-enol tautomerism, 606–7
α-Ketoglutaric acid, 611, 640–41
    643–45

Ketone bodies, 630-31
Ketones, 358-74
  nomenclature of, 362-63
  physical properties of, 363-64
Ketosis, 631
Khorana, H. Gobind, 529
Kidneys, 204, 580-81
Kidney stones, 252, 581-82
Kinase, 534
Kinetic energy, 6
Kinetic-molecular theory, 4, 128, 130, 135-37
Kornberg, Arthur, 523
Krebs, Hans Adolf, 608, 646
Krebs cycle, 608-12, 642
Kwashiorkor, 498

Lacrimal fluid, 582-83
Lactase, 590
Lactic acid, 236, 412, 454, 608, 614
Lactose, 467, 583
Lanosterol, 633
LAS detergent, 432
Lavoisier, Antoine Laurent, 17-20
Law, scientific, 18
Law of combining volumes, 106-9
Law of conservation of mass, 18, 22
Law of constant composition, 20
Law of definite proportions, 20, 22, 26
Law of multiple proportions, 20-22
Law of partial pressures, Dalton's, 139-40
L configuration of amino acids, 494
LD 50/30 days, 62
Lead poisoning, 427, 513, 541-42
Le Chatelier, Henri Louis, 124
Le Chatelier's principle, 124-25
Lecithins, 484, 628
Leucippus, 16, 24
Leukemia, 570
Leukocytes, 570
Levulose, 462
LH, 561
Librium (chlordiazepoxide), 420-21
Lidocaine, 418, 420
Ligase, 534
Light, as a form of energy, 37
Limestone, reaction of with acids, 215
Lindane, 327
Linear alkylsulfonate (LAS) detergent, 432
Line spectrum, 37-38
Lipase, 534, 589-91
Lipid, definition of, 474
Lipids, 473-92
  metabolism of, 617-36
  normal fasting levels of, 619
Lipid storage diseases, 635
Lipoproteins, 618
Liquids, 6, 151-56
Lister, Joseph, 353
Lithium carbonate, therapeutic uses of, 273
Litre, 9
Local anesthetics, 419-20
Lock-and-key theory of enzyme action, 536-37
London, Fritz, 150
London forces, 150
London smog, 264-65
Los Angeles smog, 268-69
Lowry, Thomas M., 217
LSD, 395-96
Lucretius, 17
Luteinizing hormone (LH), 561
Lyase, 534
Lye, 221
Lymph, 579-80
Lymph nodes, 580
Lysine, 595
Lysozyme, 532-33, 583

Macromolecules, 440
Malathion, 436
Malic acid, 612
Malonaldehyde, 479
Malonyl coenzyme A, 623-25
Maltase, 534
Maltose, 466-67
Manhattan project, 69
Mannose, 461
Marble, reaction of with acids, 215
Markovnikov, Vladimir V., 343
Markovnikov's rule, 343
Mass, definition of, 6
Mass defect, 76
Mass-energy relationship, 68, 76
Mass number, 49
Matter
  definition of, 5-6
  states of, 6
Measurement, systems of, 8
Mechanism, for chemical reactions, 123
Meitner, Lise, 68
Melanins, 645
Melanophore-stimulating hormone (MSH), 505
Melting point, 158
Mendeléev, Dmitri Ivanovich, 30-31, 256-57
Meprobamate, 420-21
Mercaptans, 425-26
Mercury poisoning, 427, 513
Mering, Joseph von, 413
Messenger RNA (mRNA), 526-29
Mestranol, 565
Metallic solids, 158
Metals, 86
  active, 211
  activity series of, 212-13
Methamphetamine, 410-11
Methane, structure of, 96
Methanol, physiological properties of, 345
Methedrine (methamphetamine), 410-11
Methemoglobin, 595
Methionine, 543, 644
Methoxychlor, 327
Methylene chloride, 316
Methyl salicylate, 384
Metre, 9
Metric prefixes, 8
Metric system of measurement, 9
Mevalonic acid, 633
Meyerhof, Otto, 605
Micelles, 490
Milk, 583-84
Milk of magnesia, 217
Millikan, Robert A., 29
Millimetres of mercury, definition of, 130
Minerals essential to health, 253
Miscibility, 184
Mixtures, 26
Model, scientific, 4
Models of the atom, 44
Molar heat of fusion, 158
Molar heat of vaporization, 155
Molarity, 193
Molar volume of a gas, 138-39
Mole, definition of, 110
Molecular crystals, 158
Molecule, 24
Monolayers, 490
Monomer, 442
Monoprotic acids, 207
Monosaccharide, 459
Monosodium glutamate (MSG), 501
Morphine, 389-90
mRNA, 526-29
MSG, 501
MSH, 505
Mucin, 252, 587
Müller, Paul, 322
Multiple proportions, law of, 20-22
Muriatic acid, 220
Muscone, 373
Muscular dystrophy, 552
Mustard gas, 428-29
Mutarotation, 464
Myocardial infarction, 615, 645
Myoglobin, 511-12
Myosin, 614

NAD$^+$. *See* Nicotinamide adenine dinucleotide
NADP$^+$, 556, 624-25
Naphthalene, 309-10
β-Naphthylamine, 405
Narcotic, 389
Neon, 258
Neoprene, 449

Normality, 224
19-Norprogesterone, 565
Novocaine (procaine hydrochloride), 406, 419-20
Nuclear accelerators, 55
Nuclear power, 74
Nuclear theory of the atom, 35-36
Nucleases, 648
Nucleic acids, 515-31
  base pairing in, 521-23
  constituents of, 516
Nucleoproteins, 515, 523
  metabolism of, 648-51
Nucleosidases, 648
Nucleosides, 516-18
Nucleotidases, 590, 648
Nucleotides, 516, 519-20
Nucleus, 35
Nylon, 442-43, 450

Obesity, 632
Octane number, 294
Octet rule, 90
Oils, 476
Oncotic pressure, 574
Opium, 415
Orbitals, electronic, 42-44
Organic chemistry, definition of, 256
Organophosphorus compounds, 434-36
Ornithine, 535, 647-48
Ornithine cycle (urea cycle), 646-48
Orthomolecular medicine, 558
Osmosis, 198-99
Osmotic pressure, 199, 242
  and fluid balance in body, 200-201, 573-75
Osteomalacia, 551
Oxaloacetic acid, 609-10, 612, 641, 644-45
Oxalosuccinic acid, 349, 611
Oxidase, 534
Oxidation, 165-82
  definitions of, 170
  occurrence of in electrolysis, 244
Oxidation numbers, 167-71
Oxidative deamination, 639-40
Oxidative phosphorylation, 612-14
Oxidizing agents, 173, 175-80
Oxygen, properties of, 166-67, 175, 261-62
Oxygen debt, 614
Oxytocin, 504-6, 561
Ozone, 179, 263, 543

Packer, Lester, 552-53
Pain relievers, 392-93
Palmitic acid, 378
PAN, 269, 543
Pancreatic juice, 591
Pantothenic acid, 554, 556
Nerve poisons, 435-36
Neutralization reaction, 213-14
Neutron, 36, 41, 48
Niacin, 395, 554, 556
Niacinamide, 395
Nicholson, William, 26-27, 238
Nicotinamide, 395, 554
Nicotinamide adenine dinucleotide, (NAD^+), 555-56
  in metabolic processes, 606-10, 612-13, 622, 627, 631
Nicotinamide adenine dinucleotide phosphate ($NADP^+$), 556, 624-25
Nicotine, 372, 416
Nicotinic acid, 395, 554
Niemann-Pick disease, 635
Ninhydrin, 408-9
Nitrogen balance, 639
Nitrogen fixation, 265-68
Nitrogen oxides, 270-71
N-Nitrosoamines, 408
Noble gases, 257-59
Nomenclature, IUPAC, 286-92
2-*cis*-6-Nonadienal, 373
Nonmetals, 86
Nonsaponifiable lipids, definition of, 486, 632
Norepinephrine, 410, 561, 594
Norlutin, 565
Papain, 544
Paracelsus, 2
Paraffins, 297
Parathion, 436
Partial pressures, law of, 139-40
Pauling, Linus, 73-74, 509, 522, 558
PCB, 330-31, 452
Pellagra, 555
Penetrating power, of nuclear radiation, 59-60
Pentobarbital, 413
PEP, 607
Pepsin, 534, 539-40, 588-89
Pepsinogen, 540, 589
Peptidase, 534
Peptide, definition of, 502
Peptide bond, 500
Peptones, 589
Periodic table, 30-31
Peritonitis, 595
Permanent wave, 429
Pernicious anemia, 589
Peroxides, 168
Peroxyacetyl nitrate (PAN), 269, 543
Perspiration, 582
Petroleum, 292-95
pH
  definition of, 229
  effect of tooth decay and bone growth on, 251-52
  scale of, 227-30
Phenacetin, 392
Phenobarbital, 414
Phenol, 352, 594
Phenols, 352-53
Phenylalanine, 642, 644-45
Phenylalanine hydroxylase, 644
β-Phenylethylamine, 410-11
Phenyl group, 385
Phenylhydrazones, 369-70
Phenylketonuria (PKU), 644-45
o-Phenylphenol, 353
Phenylpyruvic acid, 645
Phenyl salicylate, 388
Phillips, David C., 533
Philosopher's stone, 2
Phosgene, 221
Phosphatase, 626
Phosphatides, 483-84
Phosphatidic acid, 626
Phosphatidylcholine, 628
Phosphatidylethenolamine, 627-28
Phosphatidylserine, 629-30
Phosphines, 434
Phosphoenolpyruvic acid (PEP), 607
Phosphoglyceric acid, 644
Phospholipids, 483-85
  biosynthesis of, 627-29
Phosphor, 58
Phosphorylase, 603
Photochemical smog, 268-69, 543
Photoscan, diagnostic uses of, 65
Photosynthesis, 7, 181, 597
Phthalates, 452-53
Physical properties, definition of, 26
Physiological saline, 200
Picric acid, 352
Piperidine, 412
PKU, 644-45
Plasma (blood), 570-71
Plasma (referring to a mixture of charged particles), 77
Plasmolysis, 199
Plaster of Paris, 2, 187
Plastic, definition of, 446
Plasticizers, 451-53
Plastics, 440-57
Platelets, 570
Pleated sheet conformation, 508-9
Polar bonds, 91-92
Poly(acrylonitrile), 445, 455
Polyamides, 443, 450
Polychlorinated biphenyls, (PCBs), 330-31, 452
Polycythemia, 570
Polyesters, 443, 450
Polyethylene, 444, 446-47
Polymers, 440-57
  biomedical, 453-54
Poly(methyl methacrylate), 445
Polypropylene, 444-46
Polyprotic acids, 208
Polysaccharides, 459

Polystyrene, 444
Poly(tetrafluoroethylene), 444
Polyurethanes, 443
Poly(vinyl acetate), 445
Poly(vinyl chloride) (PVC), 444, 452, 455
Poly(vinylidene chloride), 444
Positron, 54, 65
Potential energy, 6
Prednisone, 562
Pregnenolone, 634
Pressure
  relationship of to solubility, 141
  relationship of to temperature, 136-37
  relationship of to volume, 130-34
  units of, 129-30
Priestley, Joseph, 18, 141
Procaine, 406, 419-20
Procarboxypeptidase, 591
Product, in chemical equations, 104
Proenzyme, 540
Progesterone, 374, 562-63, 634
Prolactin, 561
Proline, 644
Promazine, 421-22
Proof, of alcoholic beverages, 346
Properties, chemical and physical, 26
Propionic acid, 377-78
Propylene glycol, 351
Prostaglandins, 488-90
Prosthetic group, 511, 577
Protease, 534
Protein
  adequacy of, 498
  definition of, 502
  metabolism of, 637-51
  synthesis of, 526-29
  turnover rate of, 639
Proteins
  as blood buffers, 235-36
  structure of, 506-8
Proteoses, 589
Prothrombin, 545, 553, 572
Protium, 48
Proton, 29, 36, 48
Proust, Joseph Louis, 19-20
Provitamin, 548
Ptyalin, 534, 588
Purine, 412
Puromycin, 517-18
Putrescine, 405, 595
PVC, 444, 452, 455
Pyridine, 412
Pyridoxal, 554
Pyridoxal phosphate, 556, 640
Pyridoxamine, 554
Pyridoxol, 554
Pyrimidine, 412
Pyrophosphoric acid, 434
Pyrrole, 412
Pyrrolidine, 412
Pyruvic acid, 607-8, 610, 614, 641, 693-94

Quantum mechanics, 42, 44
Quantum theory, 38

Rȧd, definition of, 57
Radiation
  background, 59
  detection of, 58
  nuclear, 33
  protection from, 63
  units of measurement of, 56-58
Radiation sickness, 61-62
Radiation therapy for cancer, 62-64
Radioactivity, 33, 50
  artificial, 53-55
  diagnostic uses of, 64-67
  types of, 34
Radiocarbon dating, 55
Radioisotopes, medical uses of, 66
Rancidity, of fats, 478-79
Rates, of reactions, 118-23
Rauwolfia serpentina, 421
Rayon acetate, 441
al-Razi, 2
Reactants, in chemical equations, 104
Reaction rate, 118-23
Reactions, reversible, 117-18
Red blood cells, 570
Redox, 173
Reducing agents, 173, 177-78
Reducing sugars, 459, 464-65
Reduction, 165-82
  definitions of, 173
Reductive amination, 404-5
Regulatory enzyme, 539-40
Relative humidity, 140
Rem, definition of, 57
Renal threshold, 581
Replication, of DNA, 524-26
Reserpine, 422
Resorcinol, 352
Respiration, 142-43
Respiratory acidosis, 576
Respiratory alkalosis, 576
Respiratory chain, 613
Retinal, 549
Reversible reactions, 117-18
Riboflavin, 554, 556
Ribonucleic acid (RNA), 516-17, 520-21, 523, 526-29
Ribonucleoside, 517
Ribose, 460, 517
Ribosomes, 527
Rickets, 550-51
RNA. *See* Ribonucleic acid
Roentgen, Wilhelm Konrad, 32, 40, 56
Roentgen (unit of radiation), 56-57
Rowland, F. Sherwood, 321
Rubber, 448
Rubbing alcohol, 347
Rutherford, Ernest, 33-36, 54

Saccharide, 459
Saccharin, 462
Saliva, 587
Salol, 388
Salt bridges, 507
Saltpeter, 267
Salts, hydrolysis of, 230-33
Sanger, Frederick, 532, 600
Saponifiable lipids, definition of, 486
Saponification, 391
Saran, 444
Sarin, 435
Saturated fats, 475-76
Saturated hydrocarbons, 281
Saturated solutions, 190
Scheele, Karl Wilhelm, 18
Schlittler, Emil, 421
Schrödinger, Erwin, 42
Science, definition of, 3
Scientific law, 18
Scientific method, 5
Scintillation counter, 58
Scurvy, 547-48, 556-57
Seaborg, Glenn T., 70
Secobarbital, 414
Secretin, 591
Segmer, definition of, 444
Semipermeable membranes, 198, 203
Serine, 644
Serotonin, 410
Serum, 571
Serum glutamic-oxaloacetic transaminase (SGOT), 645. *See also* Glutamic-oxaloacetic transaminase
SGOT, 645
Shell, electronic, 39
Shock, 574-75
SI, 9
Sickle cell anemia, 579
Silk, 508-9
Skatole, 594
Smith, James R., 552-53
Soap, 479-82
Socrates, 415-16
Sodium chloride, effect of on blood pressure, 254
Sodium fluoroacetate, 610
Sodium glycocholate, 593
Sodium hydroxide, uses of, 221
Sodium salicylate, 388
Sodium taurocholate, 593
Sodium thiosulfate, 541
Solids, properties of, 6, 156-58
Solubility, 184
  effect of pressure on, 192
  effect of temperature on, 190-91

Solubility product constant, 249-52
Solute, definition of, 184
Solution, definition of, 184
Solutions, 183-205
Solvation, 185-86
Solvent, definition of, 184
Soman, 435
Spandex, 451
Specific gravity, 14
Specific heat, 160
Specificity of enzymes, 535-36
Spectrum
  continuous, 37
  line, 37-38
Spermaceti, 482-83
Sphingolipids, 484-86
Sphingomyelin, 484-85
Sphingosine, 485
Squalene, 633
Stain removal, 180
Standard temperature and pressure (STP), definition of, 138
Starch, 468-70
Starting materials, definition of, 104
Starvation, 631-32
States of matter, 6
  gases, 127-45
  liquids, 151-56
  solids, 156-58
Steapsin, 591
Stearic acid, 378, 622-23
Steroids, 486-87, 632-35
Stone, Edward, 388
STP, definition of, 138
Strassman, Fritz, 68
Strontium-90, 72
Structural formula, definition of, 99
Substrate, 534
Succinic acid, 611
Succinyl coenzyme A, 611
Sucrose, 468
Sugars, 458
Sulfanilamide, 433
Sulfhydryl group, 425
  in enzymes, 541-42
Sulfonal, 431
Sulfones, 430-31
Sulfonic acids, 431-33
Sulfoxides, 430
Sulfur oxides, and pollution, 264-65
Supersaturated solutions, 190
Surface tension, 152
Suspensions, definition of, 201
Symbols
  atomic or elemental, 24-25
  electron dot, 82ff
Synergism, 265
Synthetase, 534
Système International, (SI), 9
Szent-Györgyi, Albert, 614
Szilard, Leo, 71

Tabun, 435
Taurine, 593
Tautomerism, 370-71
  in sugars, 465
Tay-Sachs disease, 635
Tear gas, 583
Tears, 582-83
Technetium-99^{m}, 66
Teflon, 444
Temperature, 12
  in kinetic-molecular theory, 129
  and reaction rates, 119-21
  relationship of to volume, 134-36
Temperature scales, 11
Testosterone, 374, 362-63, 634
Tetracaine, 418, 420
Tetrachloroethane, 317
Tetraethyl lead, 295
Tetrahedral bonding, 94-95
Tetrahydrofolic acid, 556
Thalidomide, 396-97
Theory, scientific, 20
Thermonuclear reactions, 76-78
Thermosetting polymer, 446
Thiamine, 554
Thiamine pyrophosphate, 556
Thioglycolic acid, 429
Thiols, 425-29
Thionyl chloride, 394
Thiopental, 414
Thioridazine, 422
Thomson, George Paget, 27, 42
Thomson, Joseph John, 27, 29, 30, 34-35, 42
Thrombin, 535-36, 545
Thrombocyte, 570
Thymidine monophosphate (TMP), 519
Thymidylic acid, 519
Thymine, 516, 649, 651
Thyroid-stimulating hormone (TSH), 559, 561
Thyrotropic-releasing factor (TRF), 559
Thyroxine, 559, 561
Titration, 226
TMP, 519
TNT, 310
α-Tocopherol, 551-52
Tolbutamide, 600-601
Tollens' reaction, 366, 464
Torr, definition of, 130
Toxaphene, 328-29
Tracers, radioactive, 64, 67
Tranquilizers, 420-22
Transaminase, 534
Transamination, 640-41, 643
Transferase, 534
Transfer RNA (tRNA), 527-29
Transition elements, 275-77
TRF, 559
Tricarboxylic acid cycle (Krebs cycle), 608-12, 642
Trichloroethanes, 317
2,4,5-Trichlorophenoxyacetic acid, 33
Triglycerides, 475-76
Triolein, 475
Trinonal, 431
Tripalmitin, 475
Triphosphoric acid, 434-35
Triprotic acids, 207
Tris(2,3-dibromopropyl)phosphate, 451
Tris(hydroxymethyl)aminomethane, 407
Tristearin, 475
Tritium, 48, 77
tRNA, 527-29
Trypsin, 535, 540, 590-91
Trypsinogen, 540, 590-91
Tryptophan, 543, 594
TSH, 559, 561
Tyndall effect, 201
Tyramine, 594
Tyrosine, 594, 644-45

UDP, 602
UMP, 519
Unit cell, 156
Unsaturated fats, 477-78
Unsaturated hydrocarbons, 298
Uracil, 517, 649, 651
Uranium, radioactivity of, 32-33
Urea, 413, 535, 648
Urea cycle, 646-48
Uric acid, 649, 651
Uridine, 518
Uridine diphosphate (UDP), 602
Uridine monophosphate (UMP), 51
Uridylic acid, 519
Urine, 580-82

Vaccine, 575
Valence, definition of, 97
Valence shell, 82
Valence shell electron pair repulsion theory (VSEPR), 44, 94
Valeric acid, 381
Valium (diazepam), 420-21
Van der Waals, Johannes D., 150
Van der Waals forces, 150
Vanillin, 352
Van Slyke method, 408, 499-500
Vaporization, 152-56
  heat of, 155
Vasopressin, 504-5, 561
Villi, 590-91
Vinyl chloride, 318
Viscosity, 151-52
Vision, chemistry of, 548-50
Vitamin, definition of, 547
Vitamin A, 337, 548-50

Vitamin B complex, 553-56
Vitamin B_1, 554
Vitamin B_2, 554
Vitamin B_6, 554, 556
Vitamin B_{12}, 277, 555-56, 589
Vitamin C, 556-58
Vitamin D, 337, 550-51
Vitamin E, 551-53
Vitamin K, 553
Vitamins, 547-58
  water-soluble, 553-58
Volta, Alessandro, 238
Volume
  relationship of to pressure, 130-34
  relationship of to temperature, 134-36
Von Hohenheim, Theophrastus Bombastus, 2
VSEPR, 44, 94
Vulcanization, 449

Water, 159-63
  molecular structure of, 93-94
  as a solvent, 162-63
Water-soluble vitamins, 553-58
Watson, James D., 522-23
Wave equations, 42-43
Waxes, 482-83
Weight, definition of, 6
White blood cells, 570
Wilhelmy, Ludwig, 122
Wilkins, Robert, 421
Willstätter, Richard, 416
Wöhler, Friedrich, 5
Wood alcohol, 345
Wool, 509

Xanthine, 648-49
Xenon tetrafluoride, 259
Xerophthalmia, 549-50
X rays, 32, 40
  diagnostic uses of, 249
Xylocaine (lidocaine), 418, 420

Zwitterion, 494
Zymase, 534

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